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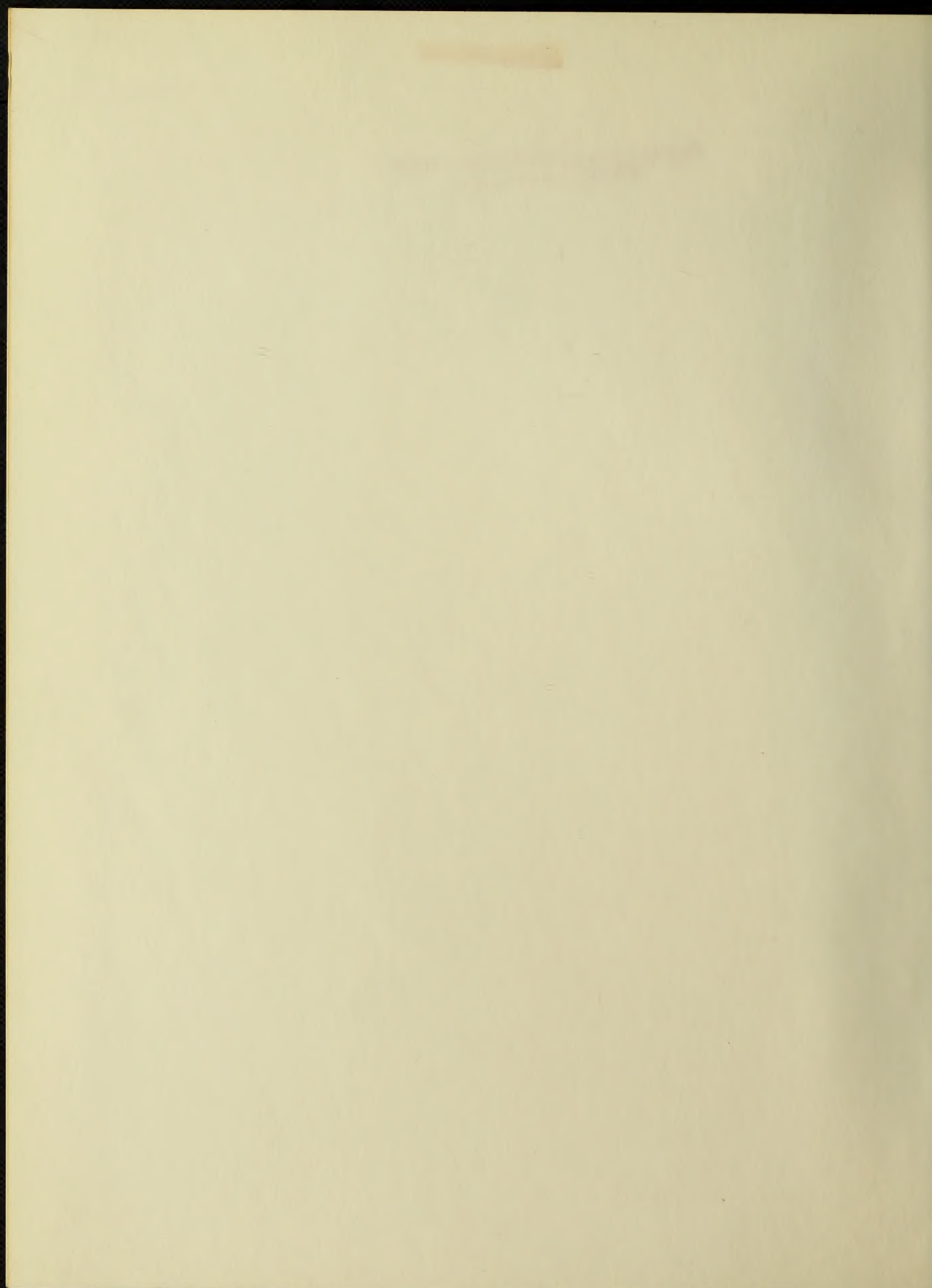
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~~Psychopharmacology~~

Psychopharmacology ABSTRACTS

1962
vol. 2 no. 7

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U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results.

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U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
Public Health Service
National Institutes of Health
National Institute of Mental Health
Bethesda 14, Maryland

PSYCHOPHARMACOLOGY ABSTRACTS

Volume 2, Number 7

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PSYCHOPHARMACOLOGY ABSTRACTS

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REVIEWS, SUMMARIES, BIBLIOGRAPHIES,
AND GENERAL ARTICLES AND BOOKS

1369 Laborit, H. Mechanismen biologischer Regelung von Stoffwechselvorgängen unter dem Einfluss der Umwelt und pharmakologischer Stoffe. [Mechanisms of the biological regulation of metabolic processes under the influence of the environment and drugs.] *Ärztliche Forschung*, 1962, 16, 383-402.

A broad general discussion is given on the regulatory role of DPN and TPN in carbohydrate metabolism, in which the author maintains that disruption of oxidative phosphorylation forms a common basis for a wide variety of pathological conditions, and that the basic mechanism of action of a wide variety of drugs is either an oxidative or reductive effect with respect to TPN. Thus, drugs which oxidize TPN, such as the phenothiazine derivatives, favor the entry of glucose into the pentose phosphate shunt and exert hypnotic, hypokalemic, lipidogenic, galactorrheic, hypotensive and hyperthermic effects, while drugs which reduce TPN, such as the MAO inhibitors, favor the Embden-Meyerhoff scheme and have analeptic, hypertensive and antiketogenic properties. This theory is supported by a review of the literature on the effects of drugs on blood pressure, the physiology of sleep, anesthesia and analgesia, including EEG studies, the biochemistry of fatigue, shock, mental illness and diabetes, age and arteriosclerosis, artificial hibernation and the biology of cancer. (47 refs.)

Hôpital Boucicaut
78 Rue de la Conversion
Paris 15, France

1370 Capparell, Homer V. Drug therapy in mental illness. *Pennsylvania Medical Journal*, 1962, 65, 899-905.

Agents used as adjuvants in the care of disturbed patients include the following: reserpine, phenothiazine derivatives (chlorpromazine, promethazine, promazine, trifluoperazine, etc.) and antidepressants (iproniazid, isocarboxazid, phenelzine, imipramine, nialamide, tranylcypromine, etryptamine, etc.). Side effects from phenothiazines include extrapyramidal reactions and jaundice, while antidepressants

may cause hypotension or hepatotoxicity. The physician must exercise judicious judgement in selecting drugs, due to the notorious lack of drug specificity for a given complex of symptoms. Such tranquilizers as meprobamate or chlordiazepoxide are very valuable in office practice in treating minor emotional disorders. (No refs.)

[No address]

1371 Nettleship, A., & Lair, Charles V. Time and disease. *Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology*, 1962, 23, 106-115.

The perception of time and its relationships to disease processes are reviewed. Topics include theoretical considerations, medical and psychiatric contributions to time perception, modifications of the sense of time by neuropsychological conditions and the assessment of ambiguity in the passage of time. Hashish and alcohol effects are mentioned. Four areas of psychological research that have contributed to an understanding of the concept of time (either directly or indirectly) are discussed, i.e., maturation, learning, perception and sensory deprivation. The intact neural mechanism is considered basic to man's interpretation of time. (32 refs.)

Laboratory Service
VA Hospital
Fayetteville, Ark.

1372 Gilbert, Gordon J. Reaction to glutethimide. *New England Journal of Medicine*, 1962, 266, 1119. [Letter]

A physician questions the proper classification of 3 previously reported cases of prolonged glutethimide administration (Zivin and Shalowitz, 1962). These patients may have really shown withdrawal symptoms, although they were purportedly still receiving the medication. Similar symptoms (grand mal seizure, fever, delirium, confusion and hallucinosis) have been noted in patients suffering from phenobarbital, meprobamate or

alcohol withdrawal.

Neurology Service
U.S. Air Force Hospital (MATS)
Travis Air Force Base, Calif.

1373 Ross, Paul. A.P.C. as a cause of renal disease. *Medical Journal of Australia*, 1962, 2, 539-543.

This is a review of the evidence linking phenacetin abuse to renal damage. Topics discussed include: the fate of phenacetin in the body, toxic effects on red cells, toxic effects on the kidney, prevalence, diagnosis, prognosis and treatment. Deleterious effects due to analgesics may be a consequence of a preexisting renal disease. Some contaminating ingredient in the analgesic may be responsible for causing renal damage. How much phenacetin is likely to cause renal damage and what amount is likely to be fatal? There seems to be a sufficiently probable causal relationship between phenacetin and renal disease, even in the absence of unequivocal experimental proof, to warrant the recommendation that this drug be made available only on a prescription basis. (36 refs.)

[No address]

1374 Berblinger, Klaus W. Psychiatric perspectives in medicine. *Psychosomatics*, 1962, 3, 106-119.

Psychiatric treatment routinely revolves around initial referral to the psychiatrist followed by hospitalization with subsequent psychotherapy, including directive therapy (advice and counseling, hypnosis and hypnotherapy) and nondirective techniques (medical psychotherapy, analytically oriented psychotherapy and psychoanalysis). Psychopharmacological treatment encompasses utilization of the major tranquilizers (phenothiazine derivatives, e.g., chlorpromazine), rauwolfia alkaloids, minor tranquilizers (meprobamate), barbiturates, sedatives and hypnotics, bromides, nonbarbiturate sedatives and hypnotics (glutethimide) and stimulants (amphetamines and hydrazines). Admoni-

tions are given for the care and handling of suicidal patients (evaluation of suicidal risk, general assessment, criteria for imminent suicide and prevention of impending suicide), homicidal patients (those with impaired control, i.e., epileptics, paranoids, and severely depressed patients) and addicted patients. Posttraumatic psychiatric reactions and iatrogenic illness are also discussed. (24 refs.)

[No address]

1375 Stokvis, B. Psychotherapie und Psychopharmakologie bei Psycho- und Somatoneurotikern. Heil-Erfolge oder Schein-Erfolge? [Psychotherapy and psychopharmacology in psychoneurotic and psychosomatic diseases. Therapeutic response or placebo response?] *Acta Psychotherapia*, 1962, 10, 246-264.

A brief, critical discussion of the excessive use of psychotropic drugs for neurotic complaints under the influence of mass publicity, and a review of the criteria for establishing the existence of a placebo response, are followed by a report of a study on the possible "placebo effect" of psychotherapy. The techniques of individual and group psychotherapy are reviewed and the requirements for a study of its true effectiveness are outlined. A comparison of the results in 105 neurotic patients given either supportive or analytical psychotherapy, and a follow-up study of 245 patients with psychosomatic disorders, 113 of whom received psychotherapy, indicated that there is little difference in effectiveness between various types of psychotherapy and that psychotherapy did not seem to alter the prognosis in psychosomatic illness. The author warns, however, against the premature drawing of unfavorable conclusions with regard to psychotherapy. (27 refs.)

Psychosomatic Center
University of Leiden
Leiden, The Netherlands

1376 Impastato, David J. Effect of drug therapy on the frequency of EST. *American*

Journal of Psychotherapy, 1962, 16, 387-396.

The following topics are included in a discussion of the merits of ECT (EST) as opposed to drug therapy: frequency of ECT, deleterious effects of ECT (fractures, memory changes, the aura of fear, tension and anxiety, decreased mortality), disadvantages of drug therapy (delayed therapeutic response to antidepressant drugs, inferior therapeutic results with drug therapy, toxic effects), advantages of ECT (rapid response, increased efficacy, increased safety, less time and expenditure required) and advantages of drug therapy (greater familial acceptability, no loss of working time, no memory disturbances). ECT is used 25-50% less since the institution of the antidepressants. ECT is classified as being ultimately superior to drug therapy. Drug treatment is contraindicated in suicidal patients.

Department of Psychiatry
New York University School of Medicine
New York, N. Y.

1377 Moe, Robert, Bagdon, Robert E., & Zbinden, Gerhard. The effect of tranquilizers on myocardial metabolism. *Angiology*, 1962, 13, 4-12.

A series of studies on the effects of tranquilizers on myocardial metabolism in various animals in vivo and in vitro is reviewed. Topics discussed included the following: the typical peripheral mode of action, effect of these tranquilizers on heart and brain bioamines, the rate of O₂ uptake in in vitro preparations of rat heart slices, lactic acid content in total heart muscle and contractile responses of electrically driven auricles; in vivo effects on myocardial necrosis induced by isoproterenol, CNS and autonomic function. Drugs mentioned include chlorpromazine, chlordiazepoxide and meprobamate. Direct effects of chlordiazepoxide and chlorpromazine upon the myocardium and associated vascular system appeared to be of a transitory antiadrenergic nature. (17 refs.)

Department of Cardiovascular Pharmacology
Hoffmann-LaRoche, Inc.
Nutley 10, N. J.

1378 Paget, G.E. Limitations of animal tests to detect sensitization reactions in man. *Proceedings of the Royal Society of Medicine*, 1962, 55, 9-11.

The limitations of animal tests to detect sensitization reactions in man are discussed. The principles upon which screening tests are usually based are analyzed. Extrapolation of meaningful results to human therapeutics is often handicapped by species differences in the absorption, metabolism and transport of a particular drug, as well as inherent differences in disease processes. Opinions on sensitization phenomena, e.g., chlorpromazine-induced cholestatic jaundice, and conventional side effects are elucidated. The probability of truly effective animal screening at human sensitivity levels in view of our inadequate present knowledge of important related processes, is viewed pessimistically for the immediate future. (2 refs.)

[No address]

1379 *Medical Times*. A plea for the placebo. *Medical Times*, 1962, 90, 161-162.

The use of the placebo in the typical double-blind trial situation is contrasted with its therapeutic utility in medical practice. The placebo can be, under certain circumstances, more powerful than the active drug in alleviating the patient's symptoms and becomes a true therapeutic agent. (No refs.)

Manhasset, L. Is., N. Y.

1380 Krauss, Stephen. Insulin therapy. *Lancet*, 1962, 2, 382. [Letter]

A combination of insulin and a ganglion-blocking hexamethonium derivative [no details] decreased the coma induction period to less than one half and also the dose

required to produce the 1st coma to one third in 147 patients treated with modified insulin shock from 1956-1960 at the University of Vienna Psychiatric Hospital (Hift 1961). The method was safe, with an occasional case of orthostatic collapse from hypotension constituting the only detriment. Neither clinical results nor criteria for selection of suitable cases has been forthcoming. Prior to the initiation of this combination, hyaluronidase was substituted for the hexamethonium derivative, but clinical results were variable and not very significant. (4 refs.)

[No address]

1381 Scocchera, Licia Fides. Un nuovo derivato fenotiazinico: la dixirazina. [A new phenothiazine derivative, dixyrazine.] *Clinica Terapeutica*, 1962, 23, 375-382.

Dixyrazine inhibition of CR's in rats, effects on reducing benzadrine mortality, its anti-apomorphine and antihistamine activities are outlined. Dixyrazine potentiation of hexabarbital, hypotensive effects, behavioral effects and psychomotor activity are given in comparison to promazine and chlorpromazine. Its action is somewhat similar to these latter compounds but its toxicity is less. Its low toxicity makes it valuable for long-term therapy and the agent has been used clinically for dyspepsia and similar conditions, cardiovascular pathological states, pyrosis, spasms, vomiting, colitis, asthma with a nervous component, psychoneurosis, especially anxiety, insomnia and depression. In man the average dosage which produces tranquility is 20-150 mg per day. (8 refs.)

[No address]

1382 Symmers, W. St. C. The occurrence of angiitis and of other generalized diseases of connective tissues as a consequence of the administration of drugs. *Proceedings of the Royal Society of Medicine*, 1962, 55, 2-28.

The occurrence of angiitis and connective tissue disease as a consequence of drug administration is reviewed and analyzed.

Topics discussed include the relationship between angiitis, anaphylactoid purpura, thrombotic purpura and other collagen diseases, sensitization to drugs, and 2 "collagen-disease-like" syndromes that occur in association to drugs. Promazine and chlorpromazine were mentioned, among others, as possibly responsible for some of these conditions. The possibility of a drug-induced condition should be considered, even though there does not seem to be a clearly established relationship between drug allergy and collagen disease. (4 refs.)

[No address]

1383 Berblinger, Klaus W. Psychiatric perspectives in medicine—Part II. *Psychosomatics*, 1962, 3, 42-52.

The full gamut of psychiatric classification is presented in an attempt to redefine and stabilize current nomenclature. Neurotic reactions are categorized as follows: simple nervousness, acute anxiety state, tension state, anxiety neurosis, hysterical disorders (conversion reaction), phobic-obsessive states, obsessive-compulsive reactions, neurasthenia and hypochondriasis. Reactions designated as psychotic include: acute organic brain syndromes, sub-acute and/or chronic organic brain syndromes, the schizophrenias, pseudoneurotic schizophrenia and depressive reactions, encompassing immediate, delayed and anticipatory grief reactions, reactive depressions, depressions of nebulous genesis, involutional depression, overtly psychotic depressions, cyclic depressions and depression/masking inchoate schizophrenia. Psychophysiological stress reactions and the sociopathic disorders are also discussed. Parenteral use of thorazine is indicated during manifestation of considerable excitation or agitation. (No refs.)

[No address]

1384 London, D.R., & Milne, M.D. Dangers of monoamine oxidase inhibitors. *British Medical Journal*, 1962, No. 5321, 1752. [Letter]

Potentiation of pethidine by MAO inhibitors

with serious consequences has been reported in 14 different cases (including 3 deaths) culled from the literature. This drug combination may be administered accidentally. Prompt acidification of the urine coupled with increased diuresis increases the chances of recovery. Urinary excretory levels of unchanged pethidine must be elevated from 1 to 4% to exclude massive toxicity, and acidification of urine is 1 method of facilitating such excretion. The basic mechanism for pethidine potentiation involves a reduction in the rate of metabolic inactivation of pethidine by microsomal enzyme systems within liver cells, resulting in the accumulation of highly toxic metabolites. (11 refs.)

Westminster Medical School
London S.W. 1, Great Britain

1385 Ström-Olsen, Rolf. Insulin therapy. *Lancet*, 1962, 2, 47. [Letter]

Deep insulin therapy is advocated, and a physician explains the special department at Runwell Hospital which was constructed in the treatment block primarily to facilitate such therapy. Reduction of the number of attending nurses is accomplished by employing beds with padded sides, thus requiring only 2-3 nurses for every 6-8 patients undergoing treatment. (No refs.)

Runwell Hospital
Wickford, Essex
Great Britain

1386 Israels, M.C.G. Drug agranulocytosis and marrow aplasia. *Proceedings of the Royal Society of Medicine*, 1962, 55, 36-38.

Drug-induced agranulocytosis and marrow aplasia is reviewed in relation to many different types of drugs. The former condition was caused on occasion by tranquilizers, i.e., chlorpromazine [dosage unspecified], promazine (150-600 mg/day), imipramine (225 mg/day), meprobamate [dosage unspecified] and pectazine (75-150 mg/day). Most cases were not fatal and recovery often resulted after withdrawal; in other instances

antibiotics, transfusions and corticoid therapy were used. (18 refs.)

Royal Infirmary
Manchester, Great Britain

1387 British Medical Journal. Today's drugs. *British Medical Journal*, 1962, No. 5321, 1751. [Editorial]

Anileridine, a potent synthetic analgesic, resembles pethidine and, to a lesser extent, morphine. It is 2 1/2 times more potent than pethidine, remains active when administered orally and exerts a far less profoundly depressant effect upon the respiratory system and blood pressure than does morphine. It possesses a weak sedative effect and transient action. Caution is indicated in patients with impaired hepatic function. The tendency toward addiction is doubtlessly comparable to that evinced by other potent analgesics. The drug should be widely useful in treating chronic pain, postoperative pain, biliary and renal colic and may be of value in obstetrics. (No refs.)

British Medical Association
Tavistock Square
London W.C. 1, Great Britain

1388 Braceland, Francis J. Modern trends in psychiatry. *Virginia Medical Monthly*, 1962, 89, 75-82.

The role of psychiatry in society is discussed, from its initial relegation to the position of medicine's stepchild to its present all-pervading influence. Early psychiatry emphasized patient isolation, but even Kraepelin's concepts afforded a means of restoring order to the welter of doubt and confusion that cloaked mental illness. World War II precipitated increased rapprochement between psychiatry and medicine. Undifferentiated and paranoid schizophrenia, depression and character disorders predominate in psychiatric practice today. Rehabilitation procedures will eventually stem from community recognition of a common need. A comprehensive plan encompassing community service clinics, guidance

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centers, general hospital inpatient and outpatient facilities will do much to diminish the chronicity of severe mental illness. Familial acceptance is an important factor in rehabilitation procedures. (2 refs.)

200 Retreat Avenue
Hartford, Conn.

1389 Lebensohn, Zigmund M. American psychiatry—retrospect and prospect. Georgetown Medical Bulletin, 1962, 16, 3-19.

A comprehensive report on American psychiatry includes the following topics: early foundations of American psychiatry, moral treatment, indifference preceded by a morass of dirt, filth, overcrowding and isolation from medicine, the 4 cornerstones of modern psychiatry (i.e., neuropathology, neurophysiology, psychology and psychodynamics), the somatic therapies including insulin, metrazol, ECT and the tranquilizers, the influence of psychoanalysis on American psychiatry, and, conversely the influence of American psychiatry on psychoanalysis, research in psychiatry, American psychiatry, American attitudes and the law and the ultimate outlook for American psychiatry. (18 refs.)

Department of Psychiatry
Georgetown University School of Medicine
Washington, D.C.

1390 McBride, W.G. Teratogenic effects of drugs. Medical Journal of Australia, 1962, 2, 1001. [Letter]

Cautious and careful, objective evaluation is urged before ascribing teratogenic effects to a drug. Issue was taken with certain authors who had attributed possible congenital malformations to the maternal intake of phenmetrazine or ancroxin (meclozine and pyridoxine) during pregnancy. The 2.5% incidence of such malformations in patients taking ferrous salts, and 2-3% in patients receiving no drugs, were cited. Unfavorable observations should be reported, but incrimination in causing congenital abnormalities should

be the result of a critical analysis; patients should not be alarmed unnecessarily by uncritical accusations against drugs. (2 refs.)

143 Macquarie Street
Sydney, Australia

1391 McCutcheon, A.D. Phenacetin. Medical Journal of Australia, 1962, 2, 976-977. [Letter]

Shaw's (1962) opinion that evidence concerned with phenacetin toxicity is "poor" is contradicted. The affirmative evidence from Scandinavia, Switzerland and Germany was considered extensive and convincing; the small amount of contradictory evidence in experimental animals may not even be applicable to humans. Although only a few Australian papers have called attention to this type of toxicity, it was expected to become more apparent to the now alerted medical community. (2 refs.)

Baker Medical Research Institute
Melbourne, Australia

1392 Neil, W.H. Influence of drugs on driving. Texas State Journal of Medicine, 1962, 58, 92-97.

This detailed analysis of the effects of drugs on driving stresses the scarcity of statistical data on this important topic. Areas and drugs discussed include alcohol, narcotics (morphine, codeine and pethidine), hypnotics and sedatives (pentobarbital, amobarbital, secobarbital and thiopental), tranquilizers (chlorpromazine and meprobamate), antihistamines, CNS stimulants (amphetamines and caffeine), antibiotics, hallucinogens (marihuana), drugs impairing visual acuity (atropine), other drugs (insulin, phenytoin, primidone, trianethadione and paramethadione and drug synergism (alcohol plus barbiturates). Except for alcohol, legislative action probably is not indicated until the influence of these medications on the accident rate can be shown to be significant, but patients should be warned of the possible dangers. (18 refs.)

1217 West Cannon
Fort Worth, Tex.

1393 Lefever, Harry. The exploration of inner space. *Medical Times*, 1962, 90, 625-631.

This is an appeal for greater emphasis on research in the realm of the mind and mental disease. Topics discussed include the characteristics and symptoms of certain psychotomimetic agents, the metabolism and properties of serotonin, a historical survey, trends in basic research and contemporary theory. Among the agents mentioned were LSD, Cannabis extracts, bufotenin, harmine, mescaline, alcohol, barbiturates, narcotics and ataractics. The complexity and importance of this field is illustrated. (21 refs.)

Chestnut Lodge
Rockville, Md.

1394 Murti Rao, D.L.N. Drug addiction in India. *Journal of the Indian Medical Association*, 1962, 38, 152-153. [Editorial]

The status of drug addiction in India is detailed. Drugs mentioned include opium, morphine, heroin, ganja, cocaine, barbiturates, tranquilizers and alcohol. Among the topics discussed were incidence of addiction, the medicosocial problem, the psychological and psychopathic aspects, institutionalized treatment, legal needs, education and proposal of a governmental study committee. (8 refs.)

[No address]

1395 Cawte, J.E. Neurosis in general practice: the everyday use (or non-use) of tranquilizers. *Medical journal of Australia*, 1962, 2, 378-379.

In relation to the everyday prescription of tranquilizers, patterns of prescription, the matching game (symptom to drug), the expectations of the patient and physician and the skillfulness of the physician as an interviewer are discussed. (1 ref.)

[No address]

1396 Laurence, D.R., & Webster, R.A.

Pathologic physiology, pharmacology, and therapeutics of tetanus. *Clinical Pharmacology and Therapeutics*, 1962, 4, 36-72.

Tetanus as a disease entity is fully described and explanations of the entire disease process are given. The convulsions and spasticity which characterize tetanus result from an exaggerated reflex response to afferent stimuli due to the suppression of balanced cerebral inhibition. Control of spasticity may be maintained by drugs which act at various sites along the reflex pathway: hypnotics and sedatives, general anesthetics, centrally-acting muscle relaxants and neuromuscular blocking agents. Agents currently used to ameliorate the effects of tetanus include mephenesin, 2-amino-6-methyl-benzthiazole, dicyclopropylhetoxime, meprobamate, phenothiazine derivatives, antitoxin, phenobarbital, paraldehyde, curare, etc. (412 refs.)

Department of Pharmacology
University College Hospital Medical School
London, Great Britain

1397 Cobb, Sanford. Muscle relaxants and consciousness. *World Neurology*, 1962, 3, 72-77.

The mechanisms of dulling perception, the use of curare in preventing reflex response, the use of EEG's and the processes of de-afferentation and hyperventilation of patients are discussed. Factors which help patients become amnesic in relation to surgical experience are elucidated. Mechanisms of protection from perception and memory of operative experience under the conditions of very light anesthesia and complete muscular paralysis are outlined. An incidence of surgical memory as low as 1 in 1000 is reasonable justification for the plea for a little more anesthesia and a little less relaxant. (7 refs.)

Department of Anesthesiology
University of Miami School of Medicine
Miami, Fla.

1398 Adams, Henry B. Is mental illness on the increase? *Virginia Medical Monthly*, 1962, 89, 124-130.

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Abstracts 1399-1401

Statistics on admissions to public mental institutions are analyzed and discussed with regard to: consistency of admission rates from year to year, range of differences between states, relationships among admission rates, rates of discharge, and other indices of patient movement in hospitals, the influence of sociological factors, the effects of tranquilizing drugs on rates of admission and discharge and a comparison of patient movement rates in various types of mental institutions. Effects of tranquilizers are evaluated by comparison of changes from 1950 to 1955, and it is concluded that the numerical increase in discharges has been almost identical with the increase in admissions, both figures being about 28,000. If it is legitimate to attribute the increase in discharges to the tranquilizers, it would be equally legitimate to state that the increase in admission rates was also at least indirectly attributable to the tranquilizers. Thus it is fallacious to interpret the number of persons admitted for hospital treatment as a measure of the incidence of mental illness. Finally, the author concludes that most patients are hospitalized for their maladaptive, faulty, socially disapproved patterns of personal conduct which provoke rejection from other people. Until the essential properties of the many varieties of conduct labelled as mental illness are defined, it is impossible to measure the frequency of behavioral disorders in the general population. (11 refs.)

[No address]

1399 Himwich, Harold E. Problem of specific factors in psychopharmacology. Some specific effects of psychoactive drugs. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 3-71.

The in vitro effects of psychoactive drugs are detailed, with emphasis on reserpine and analogous amine-liberating drugs, as well as iproniazid and amine-augmenting drugs. The drug effect relationships of decarboxylase and MAO are elucidated in

relation to intracellular cerebral metabolism, i.e., a discussion of possible mechanisms of drug action. (157 refs.)

Research Division
Galesburg State Research Hospital
Galesburg, Ill.

1400 Wagner, John G. Manually sorted punched card system for pharmaceutical literature. *Journal of Pharmaceutical Sciences*, 1962, 51, 481-484.

The use of 5 by 8 inch Royal McBee cards and direct coding in a hand system for pharmaceutical literature was described and illustrated. Although originally designed for use in a department of product research and development in a pharmaceutical house, the cards may be valuable for the faculty of a college of pharmacy or for processing psychological data. Use of this system for a cooperative literature searching system and a separate complete article file are discussed. (12 refs.)

Pharmacy Research Section
Product Research and Development Unit
The Upjohn Co.
Kalamazoo, Mich.

1401 Malitz, Sidney. Problems of non-specific factors in psychopharmacology. Personality. Variables and drug effectiveness. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 141-148.

Specific and nonspecific factors in psychopharmacology are discussed, beginning with the formula $E = (P \times T) \frac{1}{2} e \frac{1}{2} E_n \frac{1}{2} g \frac{1}{2} h \frac{1}{2} i \frac{1}{2} j$ where E equals drug effects, p - physiologic characteristics of the drug, T - target symptoms, e - ego strength of patient, E_n - environment of patient, g - dose and route of drug, h - personality characteristics of patient, i - expectations of the patient and j - expectations of the therapist. Ego strength can be characterized by $N = T - e$, where N is the need for drug treatment, T - severity of target symptoms and e - ego strength of subject. Many such

variables must be taken into account in determining the overall effect of drugs (6 refs.)

Department of Experimental Psychiatry
N. Y. State Psychiatric Institute
New York, N. Y.

1402 Katz, Martin M., & Cole, Jonathan O. Research on drugs and community care. *Archives of General Psychiatry*, 1962, 7, 345-359.

This review and analysis on drugs and community care encompasses home versus hospital care for schizophrenics, a study of ataractic drugs, drugs and social therapy in chronic schizophrenia, the effect of ataractic drugs on hospital release rates, predictor variables (clinical history, sociological variables and the role of personality), data collection and analytical methods, the summation of clinical results, problems in meeting requirements of research design and recommendations on methodological issues.

NIMH
Bethesda, Md.

1403 Myerson, Ralph M. Enzymes and the central nervous system. *Pennsylvania Medical Journal*, 1962, 65, 803-806.

Compatibility of various enzyme systems promotes facilitation of intermediary metabolism at the cellular level of the CNS. Congenital metabolic disorders result when discrepancies occur in normal metabolic pathways due to the absence of a single enzyme. Phenylketonuria and galactosemia are typical examples of enzyme deficiencies, the enzymes in question being phenylalanine hydroxylase and galactose-1-phosphate uridyl transferase, respectively. CSF elevation of some CNS enzymes is frequently indicative of various syndromes. In relation to the biochemistry of mental dysfunction, it is theorized that an abnormality in indole metabolism (in the breakdown of epinephrine or its precursors) may be present in schizophrenia. (No refs.)

VA Hospital
Philadelphia, Pa.

1404 Sachtleben, P. Tagung der Deutschen Gesellschaft für Kinderheilkunde in Heidelberg vom 11. bis 13. September 1961 unter dem Vorsitz von Prof. Dr. Ph. Bamberger, Heidelberg. Zerebrale Anfälle. [60th Meeting of the German Pediatrics Society in Heidelberg, Sept. 11-13, 1961 under the chairmanship of Prof. Dr. Ph. Bamberger, Heidelberg. Cerebral Attacks.] *Deutsche Medizinische Wochenschrift*, 1962, 87, 49-51.

The papers reviewed include 1 on the clinical characteristics of childhood epilepsy, 1 on the value of the EEG in the diagnosis of cerebral attacks, several on other types of childhood convulsions, and 1 on the treatment of childhood epilepsy, by Groh, in which the speaker refers to symptomatic treatment with anticonvulsive agents, vitamin B₆ and ACTH, and mentions the use of meprobamate, phenothiazine, or nialamide in the presence of accompanying emotional disorders. The importance of proper dosage and environment is emphasized. (No refs.)

Universitäts-Kinderklinik
Homburg/Saar, Germany

1405 Ippen, H. Lichtbeeinflusste Arzneimittel-Nebenwirkungen an der Haut. [Photosensitive dermatological side effects of drugs.] *Deutsche Medizinische Wochenschrift*, 1962, 87, 480-488; 544-548.

A discussion of the etiology and clinical characteristics of photosensitive skin reactions, with a comparison between photodynamic and photoallergic reactions, is followed by a review of all the drugs for which such reactions have been reported. These include drugs for both external and internal use, 1 section being devoted to phenothiazine derivatives. The author then discusses the diagnosis, prophylaxis and treatment of photosensitive drug reactions on the basis of a detailed discussion of their mechanism of action. (196 refs.)

Reviews
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Hautklinik der Medizinischen Akademie
Düsseldorf, Germany

1406 Vandierendonck, R. Proeve ener
Synthese van het Stotterprobleem (gericht
op de therapie). [Testing some theories
concerned with stuttering (with guidelines
for therapy).] Belgisch Tijdschrift voor
Geneeskunde, 1962, 18, 225-244.

As part of an extensive review on the
etiology and treatment of stuttering, based
both on the literature and on the author's
general experiences, he mentions that
the treatment of stuttering should include
psychotherapy, drugs and speech therapy,
complemented by rhythmic exercises and
unilateral kinesitherapy. Anticonvulsive
agents such as barbiturates, hydantoins or
oxazolidines should be used only in the
presence of a hereditary epileptic trait,
which is rather common in stutterers. In
other cases, tranquilizers are recommended,
particularly meprobamate, which may
even be preferable to anticonvulsants in all
cases. Favorable preliminary experiences
with chlordiazepoxide are also mentioned.
(28 refs.)

Dienst voor Spraaktherapie
Brugge, Belgium

1407 Hargrave, Michael A. Renal damage
and phenacetin. Medical Journal of
Australia, 1962, 2, 648. [Letter]

The suggestion is made that the relatively
high incidence of peptic ulcers in patients
suffering from chronic renal disease may
be due to chronic self-medication with anal-
gesics containing salicylates, particularly
phenacetin. Another thought was the pos-
sible value of a routine renal investigation
in ulcer patients. These patients might be
harboring latent renal insufficiency.
(No refs.)

Flat 4
1 Marne Street
Vaucluse, N.S.W.
Australia

1408 British Medical Journal. Mental
subnormality. British Medical Journal,
1963, No. 5324, 177-178.

The first of 4 symposia on mental sub-
normality, held at the Institution of
Child Health, University of Birmingham
on November 3, 1962, encompassed the
following topics: the biochemistry of
mental subnormality (phenylketonuria,
maple-sugar disease, galactosemia, etc.),
genetically determined disorders of
cerebration (chromosomal aberrations,
including mongolism, Turner's syndrome
trisomy 21 or 22, etc. detected by
buccal smears) fetal environment (peri-
natal brain damage, kernicterus, meningitis,
encephalitis, lead poisoning, etc.)
diagnosis (thorough physical and mental
evaluation can preclude development of
permanent deleterious sequelae), and
developmental assessment (a 4-point
scale for determining proficiency in
locomotion, hearing, speech, hand
and eye coordination, and a personal-
social rating). (No refs.)

British Medical Association
Tavistock Square
London, Great Britain

1409 British Medical Journal. Amphetamines.
British Medical Journal, 1963, No.
5324, 173.

Amphetamines (amphetamine, tranlycy-
promine and methamphetamine), hydrazines
(phenelzine, nialamide and isocarboxazid)
and iminodibenzyl derivatives (amitrip-
tyline and imipramine), are fully discussed
in their current role as antidepressants along
with principles of treatment and problems
of drug assessment. These drugs should
be tested for possible teratogenic effects.
Side effects from the above drugs are
fully enumerated. (7 refs.)

British Medical Association
Tavistock Square
London, Great Britain

1410 Keberle, H., Hoffmann, K., &
Bernhard, K. The metabolism of glutethi-
mide (Doriden). Experientia, 1962, 18, 105-111

Metabolic studies on glutethimide, a mild hypnotic, are reviewed. In dogs, glutethimide is excreted almost entirely (92-94%) in the form of metabolites conjugated with glucuronic acid with the remainder in nonconjugated form. Two pathways are involved: dextrorotatory α -phenyl- α -ethyl glutarimide is hydroxylated in the glutarimide ring while the levorotatory form is hydroxylated at the side chain. When rats were given 6 mg of glutethimide p. o. and sacrificed 50 minutes later specific radioactivity ratios for the CNS were: cerebrum 226, diencephalon 300, cerebellum 281, mesencephalon 285 and spinal cord 249. Lack of cumulative effects through complete inactivation, and rapid complete elimination of its metabolites are cited as reasons for the absence of after effects and the virtual absence of side effects. (10 refs)

Forschungslaboratorien
CIBA Aktiengesellschaft
Basel, Switzerland

1411 Knobloch, Hilda, & Pasamanick, Benjamin. Mental subnormality. New England Journal of Medicine, 1962, 266, 1045-1052.

Topics presented in relation to mental subnormality include genetic abnormalities, metabolic disorders, chromosomal aberrations including abnormalities of the sex chromosomes, autosomal aberrations, prenatal factors and maternal infection. Abnormalities mentioned included those of protein metabolism (phenylketonuria, Hartnup disease and Wilson's disease), carbohydrate disorders (galactosemia, idiopathic hypoglycemia, sucrosuria and lipochondrodystrophy), lipid disorders (infantile amaurosis, Niemann-Pick disease and the infantile form of Gaucher's disease), certain types of nonendemic goitrous cretinism, hypercalcemia, cerebro-ocular-renal disease of Lowe, nephrogenic diabetes insipidus, maple-sugar disease and congenital nonhemolytic jaundice with kernicterus. Pare et al. (1959) have suggested that 5HT decarboxylase may be

inhibited in cases of phenylketonuria. Further biochemical data are reviewed. (73 refs.)

Department of Pediatrics
Ohio State University College of Medicine
Columbus, Ohio

1412 Delay, Jean. Psychotropic drugs and experimental psychiatry. In: Wortis, Joseph [Ed.] Recent advances in Biological Psychiatry. New York: Plenum Press, 1962, 4, 111-132.

The following topics are expounded in an address emphasizing psychiatry from a historical perspective: variations in psychological "tonus", the neuroleptic syndromes, experimentally-induced states of abnormal behavior and psychodysleptic drugs as aids in treatment and diagnosis. Psycholeptic drugs are categorized as hypnotics, tranquilizers or psychic energizers, with elucidation of numerous compounds. Drug-induced psychoses manifest diverse symptomatology varying with both the drug and the individual. Psilocybin offers new avenues of therapeutic approach. A combination of chemotherapy and psychotherapy provides the most effective means of alleviating mental illness. (No refs.)

University of Paris
Paris, France

1413 Feldman, Paul E. Problems of non-specific factors in psychopharmacology. Personality. Non-drug parameters of psychopharmacotherapy. The role of the physician. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 149-158.

The role of the physician (i.e., types of therapists) is detailed. Perusal of the drug-treatment-success-records of various staff members suggested that therapists can be classified in 3 principal types: type 1 those who are outstandingly successful, type 2 those who are moderately successful, and type 3 those who are relatively unsuccessful. The hospital population involved is

fairly homogeneous, consisting primarily of patients with schizophrenic disorders and depressive syndromes. The population of therapists consisted of 21% type 1, 41% type 2 and 38% type 3. Type 1 averages significant improvement in 90% of the drug trials, type 2 in 44% and type 3 in but 4%. In spite of ample psychological data on therapists, no personality correlations in relation to success could be made. The misconception that therapeutic success with drugs is equated with lack of sophistication in dynamic psychiatry is discredited and the need for clearer delineation of the characteristics of investigators stressed. (No refs.)

Topeka State Hospital
Topeka, Kan.

1414 Beecher, Henry K. Problems of non-specific factors in psychopharmacology. Methodology. A quantitative approach to psychopharmacology. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 85-93.

The historical origins of the quantitative approach to psychopharmacology are traced, with particular regard to the need for recognition and precise development of tools for measurement and techniques in the quantitative analysis of obtained data. Indications for increased quantification prevail in studies on schizophrenia and for the determination of psychotomimetic drug effects. Progress in the realm of behavioral science necessitates development of a system which will ultimately validate predictability. Accuracy in psychopharmacology may only be achieved through a quantitative approach to sensation. (8 refs.)

Anesthesia Laboratory
Harvard Medical School
Cambridge, Mass.

1415 Hoagland, Hudson. Problems of specific factors in psychopharmacology. Discussion. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 72-82.

The work done on psychoactive drugs in relation to amine metabolism by Himwich (Abstract 1399) is discussed. The stock piling of serotonin by MAO inhibitors and its release by serotonin play a far more important role than levarterenol. Released serotonin has a striking sedative and parasympathetic effect. Schizophrenics show marked excitement and sympathetic overactivity with increased 5HIAA excretion after the administration of MAO inhibitors followed by reserpine. Enhancement of brain serotonin may have induced some reversal of drug effects. Similar experiments have been performed utilizing cats, dogs, rats and rabbits as subjects. (9 refs.)

Worcester Foundation for Experimental
Biology
Shrewsbury, Mass.

1416 Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, Pp. 174.

This book is a compilation of papers given at the Third World Congress of Psychiatry held in Montreal, Canada from June 4-10, 1961 under the chairmanship of Jean J. Delay. Nonspecific factors which interfere with a comprehensive and more accurate evaluation of the therapeutic efficacy of psychoactive drugs are discussed. Amobarbital amphetamine, chlorpromazine, ethotrimeprazine, imipramine, isocarboxazid, chlordiazepoxide, tranlycypromine, reserpine and some hallucinogens are among the prominent drugs detailed.

Research Division
Massachusetts Mental Health Center
Boston, Mass.

1417 New York State Journal of Medicine. Dystonic reactions produced by tranquilizers, New York State Journal of Medicine, 1962, 62, 559. [Editorial]

Dystonic reactions produced by the phenothiazines include tonic contractions, myoclonic unilateral or bilateral twitches in any

muscle group, hyperextension of the neck and trunk, speech difficulties, perioral tremors, mandibular tics, impaired swallowing ability and oculogyric crisis. Marked fear usually accompanies the sudden onset of dystonic symptoms, which fortunately are brief in duration and occasionally under partial voluntary control. (No refs.)

[No address]

1418 Journal of the Indian Medical Association. Treatment of psychiatric disorders of different categories. Journal of the Indian Medical Association, 1962, 38, 234-235. [Editorial]

Insulin shock treatment, ECT and tranquilizing drugs (phenothiazine derivatives, Rauwolfia preparations, meprobamate, isocarboxazid and imipramine) are used to ameliorate acute exacerbations of psychotic behavior. Psychotherapy and occupational therapy are essential to prevent recurrences. Family attitudes must also undergo modification to the extent that the patient is exposed to the beneficial effects of affection and understanding. Mental disorders are classified as organic psychoses (acute and chronic brain disorders) and psychogenic disorders (functional psychoses including affective reactions and personality disorders, psychoneurotic disorders such as anxiety, hysteria, dissociation and obsessive-compulsive neuroses, psychophysiological disorders, personality disorders and mental deficiency). The role of the mentally defective child in society is fully elucidated. Socially maladjusted individuals such as psychopaths, drug addicts and sexual deviates are discussed from a social standpoint. (7 refs.)

Indian Medical Association
Bombay, India

1419 Journal of the Indian Medical Association. MAO inhibitors in clinical practice. Journal of the Indian Medical Association, 1962, 38, 611-612. [Editorial]

MAO inhibitors which are currently in use as psychic stimulants include iproniazid, pheniprazine, isocarboxazid, nialamide and phenelzine. Postulates are promulgated for mechanisms of drug action. These drugs augment rapport and increase insight in instances of neurotic depression. Some amelioration of psychotic symptoms may be achieved. Angina pectoris also responds favorably to treatment with MAO inhibitors, especially nialamide (50-75 mg/day) which apparently exerts the least toxic effects. Side effects include over-excitement, nervousness, muscle twitching, dry mouth, constipation, bladder disturbances, orthostatic hypotension, respiratory difficulties, etc. MAO inhibitors greatly diminish the body's ability to detoxify drugs, therefore, the following drugs are contraindicated during MAO inhibitor administration: barbiturates, amphetamine, aminopyrine, acetanilid, cocaine, procaine, meperidine, alcohol, ether and phenephrine. Antihypertensives should also be prescribed with caution. Fatal cardiovascular complications have followed phenelzine and isocarboxazid therapy. (13 refs.)

Indian Medical Association
Bombay, India

1420 Lancet. Thalidomide: Part 2. Lancet, 1962, 2, 3363-337. [Editorial]

The Invalid Children's Aid Association of Britain plans to offer coordinated services to aid all parents whose babies have been maimed by thalidomide. Personalized instructions should facilitate parental acceptance and further rehabilitation. All efforts will be made to correlate learning procedures with the normal childhood developmental pattern. Greater powers of control must be allotted to the Food and Drug Administration to diminish the possibility of exposing the public to the effects of toxic drugs. Only drugs adjudged safe beyond any doubt should be administered

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during pregnancy. Stringent supervisory regulations are urgently needed to control drug distribution. (17 refs.)

7, Adam Street
Adelphi
London, W.C. 2, Great Britain

1421 Herford, Mary. Thalidomide defects. *Lancet*, 1962, 2. [Letter]

In an effort to mitigate the effects of the thalidomide disaster, a physician suggests that the pharmaceutical house responsible for developing thalidomide contribute 500,000 pounds toward training personnel to deal with problems unique to thalidomide babies and to facilitate similar endeavors related to the tragedy. Coordination of the medical profession and auxiliary services is absolutely essential for any degree of efficacy. (No refs.)

Farnam Royal
Buckshire, Great Britain

1422 Journal of the American Medical Association. Double-blind studies on obstetrical analgesia. *Journal of the American Medical Association*, 1962, 181, 333-334. [Editorial]

Drugs used as obstetrical analgesics are evaluated. The paper by Powe et al 1962 was cited as providing evidence for the importance of using a double-blind study and doing all possible to minimize bias in order to achieve a more objective and meaningful conclusion. The possible need for differentiation of sedation and analgesia when evaluating a drug is also mentioned. (3 refs.)

American Medical Association
Chicago, Ill.

1423 Lagae, J. Singultus. [Hiccough.] *Belgisch Tijdschrift voor Geneeskunde*, 1962, 18, 31-33.

The etiology, prognosis and treatment of different types of hiccoughs are reviewed. Among the therapeutic techniques suggested are various types of causal treatment and symptomatic treatment with chlorpromazine, promazine, chloralhydrate, procainamide, calcium gluconate and anesthesia of the gastric mucosa with lidocaine. (No refs.)

[No address]

1424 Walter, Kurt. Zur modernen Pharmakotherapie psychischer Störungen und Erkrankungen. [The modern drug therapy of mental disturbances and diseases.] *Deutsches Medizinisches Journal*, 1962, 13, 179-185.

As part of a post-graduate course in physical medicine, the author presents an historical review of the development of psychotropic drugs and their role in the treatment of mental illness, from the hallucinogens and early sedatives to reserpine, phenothiazines and energizers. Implications for the etiology of neurosis and psychosis and the interrelationships between mind and body are pointed out, with special emphasis on the question of the symptomatic nature of drug effects. Side effects, the relationship between side effects and therapeutic activity, and the problem of abuse are also discussed. (No refs.)

[No address]

1425 Hofmeister, A. Neodorm—ein neues Schlafmittel. [Neodorm—a new hypnotic.] *Hippokrates*, 1962, 33, 434-435.

This is a brief review of the chemical and pharmacological properties, side effects, clinical indications, dosage and general effects of pentobarbital (Neodorm) in man and animals. In addition to its analgesic and anticonvulsive properties, the principal indication for the drug is insomnia; the only contraindication is liver damage. (12 refs.)

Rodenbeckerstrasse 40
495 Minden/Westphalia
Germany

1426 Sattes. Symposion über die Pharmakotherapie der Schizophrenie. [Symposium on the drug therapy of schizophrenia.] Deutsches Medizinisches Journal, 1962, 13, 471-472.

The central themes of a 2-day symposium held in Germany in March of 1962 are discussed and brief abstracts are given of some of the important contributions from the approximately 80 participants. Particular attention was paid to the therapy-resistant schizophrenias and to residual defects remaining after successful drug treatments, as well as to the problem of maintenance therapy. A monograph is promised. (No refs.)

[No address]

1427 Rundle, A.T. Etiological factors in mental retardation. I. Biochemical. American Journal of Mental Deficiency, 1962, 67, 61-68.

Biochemical anomalies associated with mental deficiency can be divided into 3 groups: those involving abnormal carbohydrate metabolism or storage, those involving amino acid or protein metabolism and those in which a range of lipoid material is known to be defective. Galactosemia,

idiopathic hypoglycemia, sucrosuria, phenylketonuria, Hartnup's syndrome, hepato-lenticular degeneration (Wilson's disease), arginino-succinuria, cystathionuria, organoaciduria (Lowe's syndrome), congenital methemoglobinemia, maple sugar disease, and the neuropilipidoses are reviewed. (44 refs.)

St. Lawrence's Hospital
Surrey, Great Britain

1428. Rundle, A.T. Etiological factors in mental retardation. 2. Endocrinological. American Journal of Mental Deficiency, 1962, 67, 69-77.

Mental retardation based on thyroid, parathyroid or insulin insufficiency is reviewed. Hypoparathyroidism, the effects of the various sex chromosome aberrations, including the presence of supernumerary chromosomes, Turner's syndrome, Klinefelter's syndrome, nephrogenic diabetes insipidus, hypoglycemia, dwarfism, microcephalic dwarfism, cachectic dwarfism, sexual infantilism associated with mental retardation and mongolism. (87 refs.)

St. Lawrence's Hospital
Surrey, Great Britain

See also 1444, 1478, 1497

CLINICAL STUDIES

1429 Gwynne, Peter H., Hundziak, Marcel, Kavtschitsch, Joseph, Lefton, Mark & Pasamanick, Benjamin. Efficacy of trifluoperazine on withdrawal in chronic schizophrenia. *Journal of Nervous and Mental Disease*, 1962, 134, 5, 451-455.

Seventy-eight chronic withdrawn schizophrenics (mean age = 49; mean hospitalization time = 20 years) were randomly divided into 3 groups, equally apportioned as to sex, and treated with total daily doses of trifluoperazine (10 - 40 mg), chlorpromazine (100 - 400 mg) or inert placebo. Drugs were administered p.o., b.i.d. for 4 months. Benztropine methanesulfonate (2 mg. daily) was occasionally given to control side effects. Five independent evaluations, using the MSRPP Scale, were made on each patient by 3 attendants and 2 physicians in a double-blind study before the start of therapy, 2 months after the onset and at its termination. The Mann-Whitney U Test was applied to the data, i.e., significance $p < 0.05$. After 4 months of treatment, a significant decrease in withdrawal was observed between trifluoperazine and placebo ($p = 0.03$) and between trifluoperazine and chlorpromazine ($p = 0.02$). No significant differences in other behavioral areas were noted.

Research Division
Department of Psychiatry
Ohio State University
Columbus, Ohio

1430 Bradley, William F. Adjunctive use of prozine in somatic illness. *Ohio State Medical Journal*, 1962, 58, 765-768.

A group of 97 patients with organic disorders complicated by superimposed psychological stress manifested as anxiety, tension or apprehension were selected from a general internal medicine practice. Forty-seven patients aged 30-65 years received Prozine (25 mg promazine plus 200 mg meprobamate b.i.d. or t.i.d.) and 50 patients of corresponding age received inert placebo for 12 weeks. Seventy-four percent of the Prozine-treated group and 18% of the placebo group became calmer. Excessive drowsiness was observed in 8 treated and 5 placebo patients, 17 and 10% respectively.

Dosage was reduced to half a tablet to combat drowsiness, and 75% of the Prozine-treated group experienced continued serenity undisturbed by drowsiness, while 20% of placebo patients experienced similar results. Minor additional side effects included nausea, weakness, insomnia and dry throat which were not ameliorated by a reduction in drug dosage. After 2 weeks on Prozine, 67% of the patients obtained 7 or more hours of sleep per night, whereas only 44% had obtained that amount of sleep prior to medication.

Central Ohio Medical Clinic
Columbus, Ohio

1431 Myrianthopoulos, Ntinios C., Kurland, Albert A., & Kurland, Leonard T. Hereditary predisposition in drug-induced parkinsonism. *Archives of Neurology*, 1962, 6, 5-9.

A survey was made of 728 relatives of 59 psychiatric patients (schizophrenia 47, psychosis with mental deficiency 6, manic-depressive psychosis 1 and miscellaneous 5) all over 40 years of age who received phenothiazine derivatives p.o. (600 mg chlorpromazine/day in 16 patients, 75 mg prochlorperazine/day in 14, 100 mg trifluoperazine/day in 5, 12 mg perphenazine/day in 13, 100 mg promazine/day in 1 control patient, 8 mg thioproperazine/day in 3, 5 mg fluphenazine/day in 8) for 6 weeks - 6 months during which they developed parkinsonian manifestations. The survey also included 777 relatives of 67 controls who proved resistant to the potential parkinsonian effects of the above drugs. Relatives of those manifesting parkinsonian side effects yielded 13 cases of Parkinson's disease, while relatives of the controls exhibited only 3 cases. Differences were not statistically significant and further studies are necessary to determine the existence of genetic predisposition to parkinsonism precipitated by phenothiazine derivatives.

Epidemiology Branch
National Institute of Neurological Diseases
and Blindness
NIH
Bethesda, Md.

1432 Wickstrom, Jack, and Haddad, Ray. An evaluation of the muscle relaxant properties of chlordiazepoxide: A double-blind study. *The American Journal of the Medical Sciences*, 1962, 244, 23-29.

The value of chlordiazepoxide (10 mg t.i.d. p.o.) as a muscle relaxant was assessed in a double-blind study of 70 patients with painful spastic disorders associated with fractures, bone disease and musculoskeletal trauma. The patients were divided into 2 equal groups: group A received the drug and rest, heat, traction, etc.; group B received a placebo and physical therapy. Ninety-five percent of group A and 48% of group B obtained adequate relief. Four unresponsive patients from group A did not respond to further chlordiazepoxide therapy; 9 out of 19 nonresponders from group B obtained definitely superior results with the known drug. Side effects (drowsiness, dizziness and ataxia) occurred in both groups; decreasing the dosage controlled these effects in group A only. Chlordiazepoxide (25-75 mg i.m.) was also tested in 11 severe, emergency orthopedic cases; the lower dosages were used with an adjunctive opiate or strong analgesics (morphine, demerol and xylocaine). Good results were obtained in 6 patients and fair in 4; a double-blind study was not used in this case.

Division of Orthopedic Surgery
Tulane University School of Medicine
New Orleans, La.

1433 Lasagna, Louis. Personality. The relation of drug-induced changes to personality. In: Rinkel, Max [Ed.] *Specific and non-specific factors in psychopharmacology*. New York: Philosophical Library, 1962, 114-129.

Rorschach and interview data revealed an unusually high degree of psychological maladjustment in 56 young male volunteers. Three psychotics were present in the group and 2 were hospitalized either before or after the studies. Also, postoperative patients were interviewed and assessed for Rorschach signs, and the characteristics of 54 chronically ill patients classified according to placebo reaction. The nondrug variables were often as important or more

important than the drug in contributing to the net "drug reaction." The personality of patients and their attitudes were more important determinants of the response to medication (placebo in this instance) and possible direct drug effects.

Johns Hopkins University School of
Medicine
Baltimore, Md.

1434 Rebhun, Joseph. Long-term use of amine oxidase inhibitor (isocarboxazid) in hypertension. *Journal of American Geriatrics Society*, 1962, 10, 440-446.

Ten outpatients, aged 62-91 years, with refractory hypertension and depression (plus concomitant organic disease) were given isocarboxazid (10 mg/day increased to 10 mg t.i.d.) for 30-36 months. Other hypotensive agents were also administered (reserpine and chlorothiazid). Extensive laboratory tests were performed (urinalysis, cephalin flocculation, bromsulfalein, serum transaminase and nonprotein nitrogen, etc.) and blood pressure readings were determined on a weekly or bi-weekly basis. After 3 weeks of treatment, some decrease in blood pressure was noted in all patients, and a safe level was maintained in 7 for the duration of the study. Two patients gained excessive weight, manifested increased hypertension and displayed euphoric behavior. Laboratory tests remained within normal limits, with no evident hepatotoxicity. Mental depression was alleviated in all cases, as were chest pains, nausea and dizziness. Minimal transient side effects included constipation, weakness and insomnia. The hypotensive action of MAO inhibitors in general is also discussed.

205 West Pearl Street
Pomona, Calif.

1435 Gomirato, G., & Gandini, S. Considerazioni sulla dinamica del delirio primario dedotte dal trattamento con uno psicofarmaco (1, 1, 3-triciano-2-amino-1-propene). [Considerations on the dynamics of primary delirium following its treatment with a psychoactive drug - 1,1,3-tricyano-2-

Clinical studies
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amino-1-propene.] *Giornale di Psichiatria e di Neuropatologia*, 1962, 15, 1-15.

Two cases, treated with 1,1,3-iricyano-2-amino-1-propene, were detailed. Both were paranoid-schizophrenics having a delirium component. Dosage was 0.5 g t.i.d. given orally. The agent was successful in suppressing the hallucinatory and delusional factors.

Clinica delle Malattie Nervose e Mentali
Università di Siena
Siena, Italy

1436 Morrison, Benjamin O., Laburdette, Leo, & Rogers, James. Method of testing cerebral stimulant drugs for improvement in cerebration or mentation. *Medical Times*, 1962, 90, 269-274.

A method was described for testing an anal-
epic cited as Product 5032. It was tested on 18 patients with CBS (arteriosclerosis and cerebral arteriosclerosis with senile psychosis, cerebral thrombosis and cerebral vascular accidents with hemiplegia) for 6-17 weeks. Patients were evaluated objectively according to mental status work sheets for sensorium and intellect. Included were orientation, digit span, work paths, simple calculation, proverbs, the cowboy or donkey story, general knowledge and absurdities. Increases in memory and digit span should show the greatest and intelligence the least improvement. Subjectively, 48% of the patients improved. However, when evaluated objectively no improvement was demonstrable. The value of such objective testing was stressed.

Department of Medicine
Louisiana State University School of
Medicine
New Orleans, La.

1437 Oettinger, Leon, & Simonds, Robert. The use of thioridazine in the office management of children's behavior disorders. *Medical Times*, 1962, 90, 596-604.

Thioridazine (0.2 to more than 3.0 mg/kg/day) was administered to 279 ambulatory children aged 5-16 years in 4 diagnostic categories: hyperkinetic behavior syndrome

(hyperactivity, hyperirritability and short attention span); retarded with associated behavioral disturbances (IQ below 75), epilepsy (grand mal, petit mal and epileptic equivalents) and miscellaneous conditions. Patients were usually studied for at least 3 months and followed up for 24 months. Where possible, the Bender-Gestalt, Goodenough Draw-A-Man and/or Ruetters tests were utilized; evaluation was also made by parents, teachers and physicians. A partial-blind study was performed, with neither patients nor parents aware of whether drug or placebo was being used in any given case. Results obtained were good in 82 patients, fair in 87, unchanged in 72 and worse in 38. The drug was somewhat more effective in 132 patients with marked hyperactivity. Side effects (drowsiness in 16 patients, increased irritability in 6, increased hyperactivity in 6 and deteriorated behavior in 5, etc.) occurred in 38 patients, but were not of sufficient severity to require marked concern.

1405 San Marino Avenue
San Marino, Calif.

1438 Gelder, M.G., & Vane, J. R. Interaction of the effects of tyramine, amphetamine and reserpine in man. *Psychopharmacologia*, 1962, 3, 231-241.

The interaction of tyramine, amphetamine and reserpine was studied in 2 groups of patients: normal patients recovering from an acute psychiatric illness (usually affective) and chronic schizophrenics receiving reserpine for many months. Blood pressure response to i.v. tyramine (10 mg in 15 seconds) was used to measure the extent of peripheral depletion of levarterenol, and presumably central stores as well, by reserpine (4-15 mg/day). The effects of i.v. amphetamine (10 mg in 15 seconds) on reserpine side effects were noted. The effects of chlorpromazine (50 fold higher than reserpine) on the central actions of amphetamine were also noted. The amphetamine effect was estimated by the patient's mood, optimism, self-confidence, well-being, talkativeness and energy; the evaluation of reserpine was based on mood, wakefulness, energy, nausea, dizziness, tremor

and stuffiness of the nose. Reserpine produced a significant reduction in the pressor effect of tyramine. Amphetamine continued to produce euphoria and alerting after treatment with reserpine, but its effects were reduced by large doses of chlorpromazine. Amphetamine i.v. rapidly abolished symptoms produced by large doses of reserpine.

Maudsley Hospital
London, Great Britain

1439 Williams, Graham, & Cope, Ian. An evaluation of a combination of pethidine and levallorphan ("Pethilorfan") in labour. Medical Journal of Australia, 1962, 2, 499-503.

Pethidine (usually 100 mg in primiparas) and a mixture of 100 mg pethidine and 1.25 mg of the narcotic antagonist levallorphan were compared for their value during labor in 475 women; 205 received pethidine, 189 the mixture and 81 neither drug (ether or trichloroethylene was usually used.). The neonatal state was evaluated by Apgar ratings, the time taken for the establishment of sustained spontaneous respiration and the respiratory minute volume 4-6 hours after delivery. The extent of maternal analgesia was assessed on the state of consciousness and emotional state of the mother at the end of the 1st stage of labor, the degree of analgesia (judged by the nurse and patient) and toxicity. The addition of levallorphan to pethidine did not impair the degree of maternal analgesia. The state of the newborn was slightly better (82% with an Apgar rating of 7) where mothers had received levallorphan rather than pethidine (70% with 7).

Royal Hospital for Women
Sydney, Australia

1440 Leitch, Alexander., Cullen, William, & Robertson, Duncan. The treatment of mania by thioproperazine (Majepil). Psychopharmacologia, 1962, 3, 307-315.

The use of thioproperazine (15-22.5 mg/day i.m., then p.o., usually 5-10 mg t.i.d., then 1-2 mg t.i.d.) was studied in 17 hospitalized patients, 22-66 years old, with mania and hypomania, in an uncontrolled

study, for a period of up to 546 days. Some patients had received prior treatment, i.e., trifluoperazine and chlorpromazine (both i.m. and p.o.) and ECT, without any favorable response. In most cases excitement, rapid continuous talking or singing and interference with other patients was greatly reduced and brought within easy control within 24 hours. Most patients seemed normal within a few days, except for some garrulousness and mild euphoria, which persisted for 1-4 weeks but did not require any restriction of activity or special observation. Virtually all treated patients were considered much improved or recovered upon discharge (17-546 days of hospitalized treatment). There were few side effects, primarily controllable (with benzhexol, benztropine or promethazine) parkinsonism in 10 patients. Most patients continued to receive 1-2 mg thioproperazine t.i.d. after discharge.

Glenside Hospital
Bristol, Great Britain

1441 Burt, C.G., Gordon, W.F., Holt, N.F., & Hordern, Anthony. Amitriptyline in depressive states: a controlled trial. Journal of Mental Science, 1962, 108, 711-730.

Amitriptyline and imipramine (150-200 mg/day p.o. for 4-6 weeks) were administered to 73 hospitalized female depressive patients (30-70 years old), divided into 4 groups (old severe, young severe, old mild, and young mild, those below 50 years of age being considered young). Evaluation in this double-blind controlled trial was based on a rating scale for depression, an overall clinical assessment and an occupational therapy rating scale; side effects were also recorded. Amitriptyline (78%) was better than imipramine (58%) in alleviating most of the symptoms of depression, especially in the old severe group of patients. Mild side effects, tremor, dry mouth, agitation, etc., were equally prevalent for both drugs.

Royal Park Psychiatric Hospital
Victoria, Australia

Clinical studies
Abstracts 1442-1445

1442 Seager, C.P., & Bird, R.L. Imipramine with electrical treatment in depression-controlled trial. *Journal of Mental Science*, 1962, 108, 704-707.

A controlled, double-blind study of the effect of imipramine (25-50 mg t.i.d.) and placebo on ECT was performed on 43 hospitalized patients (40 females, 28-71 years old) with moderate to severe depression, retardation or agitation. A number of these patients were followed for 6 months as outpatients, while continuing to receive imipramine or placebo. Imipramine caused neither a reduction in the number of ECT treatments required nor any potentiation. However, the drug did markedly reduce the rate of relapse.

Barrow Hospital
Bristol, Great Britain

1443 Fox, Richard. Safe sedation? A controlled trial of "megimated" amylobarbitone. *Journal of Mental Science*, 1962, 108, 731-734.

Fifty-two psychiatric patients were studied who required amylobarbitol, usually 200 mg/day; included were depressives, neurotics and schizophrenics. Three identical-appearing tablets were administered in a blind study: 1 contained only 100 mg amylobarbitol, a 2nd had both 100 mg amylobarbitol and 10 mg bemegride (megimide) and a 3rd had a placebo. Dosage was 2 tablets at night, repeated once if required; each patient received a given tablet for 3 nights. Sleep, difficulty in waking, drowsiness the following morning and side effects were noted; the patient and night nurse completed questionnaires. The bemegride did not detract from the hypnotic action of the amylobarbitol nor did it cause any toxic effects. Bemegride slightly lessened the hangover effect and appeared to add to the safe use of amylobarbitol.

Bethlem Royal Hospital
London, Great Britain

1444 Parnell, R.W., & Skottowe, Ian. The significance of somatotype and other signs in psychiatric prognosis. Part I & II. *Proceedings of the Royal Society of Medicine*, 1962, 55, 707-716.

In a lengthy discussion of medical, social and physiographic factors in mental disease, statistical comparisons of the effectiveness of chlorpromazine treatment, ECT, deep insulin coma therapy, the use of reserpine and other tranquilizers are drawn. Two-hundred-and-three male schizophrenics taken from a global population of over 3,000 were analyzed in relation to those that did not. Insulin therapy results were poor, and some of the successes in the insulin group may have been influenced by the frequency of chlorpromazine treatment. Findings in women schizophrenics were similar. Comparisons were also made of therapy with and without chlorpromazine. In each case groups treated by chlorpromazine came out best and insulin therapy worst, with reserpine and ECT occupying intermediate positions.

Warneford Hospital, Oxfordshire
Great Britain

1445 Hankoff, Leon D., Heller, Boris, & Galvin, John W. The setting in psychopharmacological treatment. *Psychosomatics*, 1962, 3, 201-208.

A private psychiatric clinic and a city hospital clinic each contributed a caseload of 10 ambulatory depressed females (10 involutional depression, 4 reactive depression and 6 schizophrenic depression), aged 17-59 years, to a crossover study designed to assess the effects of isocarboxazid (10 mg, t.i.d. decreased as necessary) alternated with placebo for 2 months. Psychiatric evaluation, a self-administered adjective checklist, a blood-pressure reading and a clinical rating scale comprised assessment of clinical status. A 3rd group of 10 patients acted as controls. Global psychiatric evaluation with a 5-point scale was undertaken at the close of the study. To insure greater reliability, a 4th group of 30 female schizophrenics (mean age 42.2 years) were also treated with isocarboxazid as above. Significantly better treatment response was obtained in both office and clinic groups in comparison with a clinic placebo group. A marked hiatus was observed in the timing of improvement, however, with office patients improving in about 3 weeks and clinic patients

in about 6 weeks (with Wilcoxon's Test for paired replicates, $p < 0.01$). Profuse, minor side effects were prevalent, including various somatic complaints in placebo-treated groups and insomnia, constipation, pedal edema and dizziness characterizing isocarboxazid-treated groups. Comparable results were obtained in office and clinic patients with isocarboxazid in early depression.

Department of Psychiatry
State University of New York
Downstate Medical Center
Brooklyn, N. Y.

1446 Feinblatt, Theodore M., & Ferguson, Edgar A. Phenobarbital idiosyncrasy: avoidance by use of phenobarbital-niacin. *New York State Journal of Medicine*, 1962, 62, 221-223.

Phenobarbital idiosyncrasy, iodism and brominism result from a common mechanism, namely that of poisoning oxidative coenzymes I and II. Niacin supplies the essential portion of the pyridine nucleus necessary to reconstitute both of these coenzymes. Forty-four patients (neurosis 30, hypertension 3, insomnia 3, menopausal syndrome 2, male climacteric 2, and 4 with organic illness), aged 23-66 years with demonstrated phenobarbital idiosyncrasy (neurologic 23, cutaneous 15 and bizarre 6) received phenobarbital-niacin (average 76 mg/day, comparable to previous doses of phenobarbital) for an average of 5 weeks. In 91% of the patients, idiosyncratic reactions previously elicited by phenobarbital were completely absent when the combination was substituted. In 9%, lassitude, depression, irritability and daydreaming were equally severe on either drug. In 29 cases, symptoms of phenobarbital idiosyncrasy (depression, lassitude, pruritis, skin rash, irritability, daydreams and panic) disappeared during continued administration of phenobarbital-niacin at equivalent dosage levels.

Kings County Hospital
Brooklyn, N. Y.

1447 Maerz, John C., Lee, Howard G., & Hunter, Harry H. Psychosomatic disorders treated with trifluoperazine. *Psychosomatics*, 1962, 3, 220-222.

Sixty-six patients with various psychosomatic disorders (epigastric distress, bowel disorders, vasomotor disturbances, etc.), aged 18-88 years, received trifluoperazine (1-2 mg p.o., b.i.d. or t.i.d.) for 2 weeks to 3 months. Reassurance, counseling and other supportive measures contributed adjunctive therapy. The addition of antispasmodics or anticholinergics produced excellent remissions in those with gastrointestinal problems complicated by anxiety. Patients with rigid personality structures responded least favorably. No overt side effects could be detected. Anxiety was reduced and tension states were effectively controlled in 46 patients (70%) treated with trifluoperazine. Also some antidepressant effect was observed in menopausal patients.

Oaks Medical Clinic
Perkiomen and Highland Avenues
Oaks, Pa.

1448 Jones, Thomas H. Chlordiazepoxide (Librium) and the geriatric patient. *Journal of the American Geriatric Society*, 1962, 10, 259-263.

Chlordiazepoxide (10-25 mg t.i.d. initially, then adjusted as necessary) was administered p.o. to 25 elderly patients (aged 52-92 years) with medical or surgical disorders who had been unresponsive to phenobarbital or chloral hydrate. Many patients [number unspecified] had moderately advanced arteriosclerosis with some degree of cardiac failure which required the constant use of digitalis preparations, and many suffered from forms of recent myocardial infarctions. Chlordiazepoxide was uniformly successful in relieving anxiety, tension and depression, in resolving emotional and behavioral crises and even in ameliorating severe personality problems. There were no serious side effects, and drowsiness related to dosage was relieved by decreased dosage or drug discontinuation. Medication was beneficial to patients with serious cardiac disorders,

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by preventing overexertion and producing a generally placating effect. Chlordiazepoxide is trustworthy and effective in treating geriatric patients whose illnesses necessitate treatment in nursing homes. Several case histories served as detailed examples attesting to drug efficacy.

2713 Argonne Road
Millwood, Washington

1449 Bertucelli, L. Esperienze terapeutiche con un derivato fenotiazinico: la mepazina. [Therapeutic experiences with a phenothiazine derivative, pecazine (Mepazine)]. *Giornale di Psichiatria e di Neuropatologia*, 1962, 15, 495-517.

The antidepressive and anxyolytic effects of pecazine (average daily oral dose 150-400 mg) were detailed in 32 psychiatric case histories. Diagnoses included depression, hypomania, neurosis, confusional and psychomotor agitational syndromes, chronic alcoholism, etc. Chlorpromazine was also used in some cases. Pecazine had efficient sedative action and definite antihallucinatory activity. Antianxiety effects were consistent and some amelioration of depression was obtained. Best results occurred in the control of psychomotor agitation, confusional excitement and aggression. Poor results were obtained with endogenous depression. Side effects, e.g., slight tachycardia, modest arterial hypotension, slight drowsiness and asthenia, were infrequent and negligible.

Clinica delle Malattie Nervose e Mentali
Università di Modena
Modena, Italy

1450 Brick, Harry. Use of meprobamate in Virginia State Penitentiary - an abstract. *Virginia Medical Monthly*, 1962, 89, 480-482.

Approximately 60 male prison patients received meprobamate (400 mg/day p.o.) or placebo for 8 weeks in a double-blind study. Each man received the Rorschach Test before and after 8 weeks of medication. Posttreatment Rorschach results implied that medication reduced neurotic tension

and anxiety factors up to 30%, while 5% reduction occurred in the placebo group. Medication produced a positive result in 80% of the drug group and 27% of the placebo group. No adverse effects or allergic reactions were noted and no indication of addiction appeared. At half the recommended dosage meprobamate reduced anxiety and tension as well as neurotic patterns in the penitentiary. Further research in this area is indicated. Previously published pilot studies provided the impetus for the present work.

Department of Mental Hygiene and
Hospitals
Richmond, Va.

1451 Jones, Carroll C. Clinical results with a new hypnotic (chlorhexadol). *Current Therapeutic Research*, 1962, 4, 327-329.

Chlorhexadol [dosage unspecified] and a placebo were used in a double-blind study in 40 hospitalized patients with an average age of 43 years, 13 of whom also received chloral hydrate (1 g/day) for several days and some of whom had gastrointestinal complaints. Each patient served as his own control in a crossover experiment, usually after 7 days. Observations were made 1-2 hours after drug administration for sleep, apparent depth of sleep (rated 1 to 4 on ease of arousal, respiration and body movements), disturbances of sleep, complaints and side effects. In 59% of the observations the patients was asleep after chlorhexadol, compared to 53% for chloral hydrate and 41% for placebo. Chlorhexadol was rated as excellent in 16 patients and good to very good in 13 in effecting sleep, compared with 10 on the placebo. Chlorhexadol had no effect in 6 patients while placebo had no effect in 15. In the 13 patients who also received chloral hydrate (11 rated excellent to good), chlorhexadol was rated excellent to good in 10. Side effects (nausea and vomiting) were noted in 1 patient receiving chlorhexadol.

John Sealy Hospital
Galveston, Tex.

1452 Stanley, W. J., & Fleming, H. A. A clinical comparison of phenelzine and electro-convulsive therapy in the treatment of depressive illness. *Journal of Mental Science*, 1962, 108, 708-710.

Thirty-eight hospitalized depressed females, 18 treated with ECT and 20 with phenelzine (15-30 mg t.i.d.), were clinically evaluated on the basis of a 9-point rating scale for depression before and after 1 month of treatment. This rating scale was based on the work of Foulds and Caine (1958) and McCall's (1958) breakdown of the Minnesota Depression Scale. Phenelzine was inferior to ECT. Side effects of ECT included transient headache, confusion and memory impairment, but there were no serious side effects. Three patients on phenelzine developed marked pedal edema on higher dosage, which responded to a reduction in phenelzine dosage and chlorothiazide [dosage unspecified]. Also 1 patient on phenelzine developed mild postural hypotension and 1 developed a transient skin rash.

Winwick Hospital
Warrington, Lancashire
Great Britain

1453 Heaton-Ward, W.A. Inference and suggestion in a clinical trail. *Journal of Mental Science*, 1962, 108, 865-870.

Nialamide (25 mg b.i.d.) was tested on 51 mongoloid patients in a double-blind study, to assess its possible influence on their mental age and behavior over a 26-week period. Evaluation was based on the Revised Stanford-Binet Intelligence Scale (form L) and a behavior questionnaire completed by the nurses. Chronological ages of these patients were 6 years 8 months to 36 years 5 months and mental ages were 1 year 7 months to 4 years 9 months. Favorable results were obtained during the 1st 13 weeks of the experiment and unfavorable results during the 2nd 13 weeks upon statistical analysis. In view of this incongruity, the data was considered inconclusive. After 20 weeks of nialamide treatment, 1 patient (the only side effect noted) developed a mild neutropenia.

Stoke Park Hospital Group
Stapleton, Bristol
Great Britain

1454 Howard, Fred J., & DeVere, Warren. Intramuscular meprobamate in the treatment of tetanus in infants and children. *Journal of Pediatrics*, 1962, 60, 421-429.

Moderately severe or severe tetanus with spastic activity constituted the presenting symptom in 15 pediatric patients 5 days to 4 years of age treated with meprobamate (80-100 mg i.m. every 3 hours) in addition to antitoxin (i.v.) and phenobarbital (4-8 mg) alternating with chlorpromazine (3-6 mg i.m.) every 3 hours. For comparison, 26 out of a series of 76 similarly afflicted pediatric patients received the same medication with the exclusion of meprobamate from the regimen. Seizures were better controlled with meprobamate than with the phenobarbital-chlorpromazine combination. Mild spasms were precipitated by injections early in the disease. Apnea required resuscitation in 3 patients. Many babies remained semicomatose for several days between spasms. Patients treated with meprobamate experienced spasms on less than half the number of days than those who did not receive the drug. Duration of hospital stay was definitely reduced in those receiving meprobamate, and less nursing care was required. Requisite amounts of phenobarbital and chlorpromazine were decreased when meprobamate was administered, thus diminishing the risk of profound respiratory depression and spastic activity. Case histories of 3 patients were presented in full to exemplify typical improvement wrought by meprobamate. A higher degree of relaxation was obtained with the drug, but the mortality rate was unaffected.

Dhahran Health Center
Dhahran, Saudi Arabia

1455 Meirsmann-Roobroeck, G.C., Rolly, G., Lateur, J., & Geirnaert, G. Methohexital. Nieuw en ultra-kort werkend intraveneus barbituraat. [Methohexital. A new and ultra-short acting intravenous

barbiturate.] Belgisch Tijdschrift voor Geneeskunde, 1962, 18, 200-209.

A review of the chemical and pharmacological properties of methohexital is followed by a brief report of a clinical trial of a 1% solution of this barbiturate for the induction of anesthesia in 258 surgical patients. Excellent results were obtained with doses of 10-100 mg i.v. (0.9 mg/kg) in a wide variety of surgical procedures, including 41 simple operations for which methohexital was used alone and a large number of serious operations in which methohexital was followed by nitrous oxide, muscle relaxants and controlled respiration. Given alone, the drug produced unconsciousness in 20-90 seconds, lasting 3-4 minutes. It had no effect on the EEG, and mild side effects such as apnea or respiratory depression, cough, hiccough, laryngeal spasm, muscular twitch, mild hypotension and tachycardia appeared in less than 10% of the cases.

Universiteit te Gent
Ghent, Belgium

1456 Tölle, Rainer. Zur Behandlung akuter Erregungszustände bei endogenen Psychosen. [The treatment of states of acute excitation in patients with endogenous psychoses.] Archiv für Psychiatrie und Zeitschrift für die Gesamte Neurologie, 1962, 203, 85-100.

Convulsive therapy (ECT or cardiazol convulsions) was compared with chlorpromazine (150-300 mg/day i.m. or 400-600 mg/day p.o.), levomepromazine (75-300 mg/day i.m. or 150-500 mg/day p.o.), perazine (150-450 mg/day i.m. or 300-800 mg/day p.o.) and thioproperazine (30-90 mg/day i.m. or 60-140 mg/day p.o.) in 76 severely agitated female psychotics suffering from catatonic schizophrenia (42 cases), agitated depression, euphoria and restlessness, mania and manic-depressive reaction. Of the 76 patients, 29 were initially treated with convulsions, usually followed by neuroleptic therapy, while 47 received neuroleptics initially. Clinical evaluation by psychiatrists and nurses indicated that agitated and stuporous catatonics responded well to both types of

therapy; neuroleptics were also effective in pernicious catatonia, and were more effective than convulsions in the presence of marked changes in affect. Convulsive therapy, however, was more effective in restless, euphoric schizophrenics and severely depressed manic-depressives. In general, the effect of neuroleptics was more rapid and more complete than that of convulsions. The piperazine derivatives were preferred in catatonia and paranoia, but levomepromazine was superior to the other drugs in affective disorders. Combinations of levomepromazine and one of the piperazine phenothiazines were effective in many cases, with a minimum of side effects. Only 2 of the 76 patients did not respond at all, and 1 of these responded to insulin shock. Of the 47 treated with neuroleptics, 10 failed to respond immediately, but 2 responded when the drug was withdrawn and 6 of the 8 others responded to ECT.

Universitäts-Nervenklinik
Tübingen, Germany

1457 Osmond, H., & Hoffer, A. Massive niacin treatment in schizophrenia. Review of a nine-year study. Lancet, 1962, 2, 316-319.

Trials of nicotinic acid (niacin) in the treatment of schizophrenia from 1952 through 1961 are reviewed. Treatment with niacin is based on the adrenaline metabolite theory of schizophrenia. For example, of all patients treated for schizophrenia in Saskatchewan from 1952 to 1955, 73 received nicotinic acid and 98 had other treatment. The nicotinic acid group showed a distinct advantage over the others, e.g. patients who had never had nicotinic acid spent 2/5 of a year in hospital, while those who received it spent an average of 1/6 of a year. Although the vitamin has an effect even after patients stop taking it, it should be taken for a year in early schizophrenia (3-6 g/day for outpatients) and it may then be discontinued. It should be taken again as soon as symptoms return, for a duration of 5 years, continuously or intermittently. When patients in hospital do not respond to nicotinic acid or its amide, a course of 8-20 ECT's combined with

the agent often precipitates much improvement. It does not seem to affect the more chronic illnesses and even in acute illness its action is often less impressive than that of the phenothiazines. However it is a useful adjunct in the treatment of schizophrenia, both for acute cases and for the reduction of relapse rate.

Saskatchewan Hospital
Weyburn, Saskatchewan
Canada

1458 Khonchak, M. & Viktor, A. Opyt primeneniya preparata meprobamate (Andaksina) pri lechenii predmenstrual'nogo simptomokompleksa. [Experimental use of a meprobamate preparation (Andaxin) in the treatment of the premenstrual symptom complex.] *Akusherstvo i Ginekologiya*, 1962, 1, 29-31.

Meprobamate (400 mg t.i.d. or 200 mg t.i.d. plus 400 mg at bedtime, p.o.) was used in 86 cases of premenstrual tension. Treatment was usually begun 6-8 days before onset of menstruation and continued for 11 days thereafter, but in some cases a 5-day treatment period was given around the time of ovulation. Symptoms disappeared completely in 42 cases, with considerable improvement in 16, improvement in 19 and failure in 7. A particularly good response was seen in patients with symptoms of hyperexcitability. Side effects were severe in 1, moderate in 1 and mild in 7 cases, the most severe being in allergic skin reaction and fever.

Janos Hospital
Budapest City Council
Budapest, Hungary

1459 Aronson, Philip R., & Hosbach, Richard E. Chronic hyperventilation syndrome clinical results, electrocardiographic findings with chlordiazepoxide. *Angiology*, 1962, 13, 23-31.

Eleven patients with chronic hyperventilation syndrome, 4 adolescent females ages 11 to 14 and 7 adults (3 male and 4 female) aged 18 to 52 years, were treated in a double-blind study. All patients were seen

every 1-3 weeks and medication frequently changed so that either placebo or chlordiazepoxide (15-40 mg daily was administered. An alkalemia after hyperventilation, both with and without chlordiazepoxide, was consistently produced and the chloride and sodium levels were unaltered after overbreathing. Chlordiazepoxide did not affect CO₂ combining powers which tended to fall after 2 minutes of hyperpnea. Five out of the 11 were symptomatically relieved by chlordiazepoxide hyperventilation and the less common ST segment depression, appeared to be inhibited by the medication. This resulted in a normal ECG and therefore less confusion with "false positive" Master two-step exercise tests and so-called "non-specific borderline" patterns. The changes in serum potassium levels or heart rate (sympathetic effect) do not seem to explain these findings. A direct myocardial or, more likely, CNS effect is possible.

Medical Arts Building
Norwich, N. Y.

1460 Williams, Meyer, Niebel, Harold H., & McGee, Thomas F. Effects of oxanamide on anxiety during oral surgery. *Journal of Oral Surgery, Anesthesia, and Hospital Dental Service*, 1962, 20, 101-107.

The effect of oxanamide (Quiactin; 400 mg p.o.) on preoperative anxiety was tested in a double-blind placebo-controlled study involving 300 male veterans awaiting dental surgery. Evaluation was by means of the Taylor Manifest Anxiety Scale, filled out 1 hour before tooth extraction (just before administration of either the drug, a placebo or nothing). Also a special anxiety scale was filled out by the dentist post-operatively. Neither oxanamide nor placebo had any significant effect on the degree of preoperative anxiety as measured by the Anxiety Scale; both, however, produced improvement in subjective well-being and most patients seemed overtly less anxious. Dentists were unable to distinguish between oxanamide and placebo-treated patients.

Dental Service
West Side VA Hospital
Chicago, Ill.

Clinical studies
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1461 Nahunek, Karel, Rodova, Alena, Hosak, Ladislav, Jaros, Milos & Hadlik, Josef. Nialamid und seine Kombinationen mit Stoffen von Reserpincharakter (Fenoharman, Reserpin) bei der Therapie endogener Depressionen. [Nialamide and its combinations with reserpine-like substances (fenoharmane, reserpine) in the treatment of endogenous depressions.] *Deutsches Medizinisches Journal*, 1962, 13, 424-425.

Nialamide (increasing doses up to 200-400 mg/day for 7-60 days) was first tried alone in 25 patients with various types of endogenous depression. Cure or marked improvement was obtained in 8, usually within 2 weeks, partial improvement in 3, no effect in 10 and aggravation in 4. Patients with anxious depression failed to respond. Nine of the patients who did not respond were then treated with nialamide (up to 150 mg/day) plus fenoharmane (up to 200-300 mg/day) for 7 days, followed by nialamide plus reserpine (up to 2-3 mg/day) for 7-21 days. No improvement was observed with fenoharmane, and only 1 case responded to nialamide plus reserpine. There were no serious complications, the only side effects being migraine headache, insomnia, hypomania, confusion, and nausea and vomiting. Preliminary studies on the effect of 75 mg of nialamide on psychomotor function in 10 patients showed a stimulatory effect on reaction time, tapping rate, free association and arithmetic ability, which could not, however, always be correlated with subsequent clinical improvement.

Psychiatric Clinic
J. E. Purkinje University
Brno, Czechoslovakia

1462 Kieser, Jürgen. Zur Methodik der kontrollierten Hypothermie in der psychiatrischen Klinik. [The technique of controlled hypothermia in the psychiatric clinic.] *Archiv für Psychiatrie und Zeitschrift für die Gesamte Neurologie*, 1962, 203, 185-195.

In order to prevent injurious effects from the intensity of the body's own defense mechanisms, the author recommends partial neuroplegia and hypothermia in certain diseases of the nervous system,

particularly encephalitis, meningo-encephalitis, meningitis, acute exacerbations of cerebral forms of thromboangitis obliterans, and infective-toxic psychoses. Treatment, presented in schematic form, consists of premedication with a lytic cocktail (50 mg each of chlorpromazine and promethazine, and 2 cc each of pethidine and hydergin). Subsequent infusion during artificial cooling include diethazine (250 mg and 125 mg), chlorpromazine and promethazine (each 50 and 100 mg), pethidine (1 cc) and hydergin (1 cc and 1 ampule), all in suitable media containing sugars, vitamins, etc. Rapid cooling and subsequent rapid reheating of the body is stressed, since both transitional phases are fraught with danger. Proper care must be taken with respect to nutrition, hormonal substitution, mineral balance, and circulation.

Psychiatrische und Neurologische Klinik
Universität des Saarlandes
Homburg/Saar, Germany

1463 Birkmayer, W., & Neumayer, E. Die Normalisierung des affektiv-vegetativen Pegelstandes. [Normalization of the level of the affective-automatic nervous system.] *Deutsches Medizinisches Journal*, 1962, 13, 433-437.

On the basis of experience with fluphenazine (initially 1 mg t.i.d. p.o., doubled in case of need) in 110 patients with affective-autonomic arousal reactions due either to sensory or mental stimuli or organic disease, as well as a theoretical review of neurophysiology and the etiology and treatment of vegetative dystonia and autonomic lability, the authors conclude that fluphenazine is the best available regulator of the reticular formation, increasing its sensitivity threshold without entailing side reactions such as lassitude, exhaustion, or general depressive symptoms. However, the authors caution against the higher dosages, since only the rapidity, but not the effectiveness of its action, is increased. EEG studies in 20 patients showed a general increase in the alpha effect and inhibition of the arousal reaction. In organic disease, the drug

should be combined with specific therapy.

Neurologische Abteilung
Versorgungsheimplatz 1
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1464 Deleanu, M., Sirbu, A., & Asgian, B.
Luftionen in der Behandlung von Schlaflosigkeit bei psychogenen, neurotischen Zuständen. [Ionized air in the treatment of insomnia in psychogenic, neurotic cases.] Deutsche Gesundheitswesen, 1962, 17, 1329-1331.

The results of treating 100 cases of psychogenic insomnia by means of ionized air are reported. Treatment consisted of daily sessions during which the patients inhaled negatively ionized air having 300-12000 ions/ml, depending on the patient's respiratory rate, initially for 15 minutes, increasing to 40 minutes over 10-20 days. Results were favorable in 65 cases, the duration, depth, and onset of the sleep being such as to cause the patients to feel rested. A recheck of 47 of these patients 3-15 months later showed persistence of the favorable effects. In 13 patients, temporary improvement occurred, but insomnia recurred after physical trauma, intellectual overwork, or illness. In some cases, resumption of treatment again had favorable results. In the remaining cases, improvement was at best transitory. In no case did serious side effects arise, and the occasional headaches and restlessness were only temporary.

Institutul de Igiena
Cluj, Romania

1465 Kronberger, Leo. Über die Verwendung eines Langzeit-Sedativums in der präoperativen Zeit und dessen Einfluss auf die Blutgerinnung. [On the use of a long-acting sedative during the preoperative period and its influence on coagulation.] Deutsches Medizinisches Journal, 1962, 13, 14-16.

Doscalun, a long-acting sedative containing 0.1 g atropine-N-n-octyl-bromide and 0.075 g phenobarbital, was administered in the form of gelatin sustained-release

capsules to 47 patients, including 35 surgical patients who were treated with the drug 6 days before and 8 days after the operation. All seemed markedly more relaxed and even-tempered. Functional disturbances common to the operations either vanished or else were prevented. Determinations of the antithrombin-time and heparin-time in 12 of these patients showed significant prolongation and a definite prophylactic effect against thrombosis. This effect was not comparable to that of anticoagulants. An additional 12 patients, who were subjected to endoscopies only and were treated 2 days before and on the day of this procedure, showed no significant change in antithrombin- and heparin- times.

Chirurgische Universitätsklinik
Graz, Austria

1466 Gutzmann, Hermann. Über die Möglichkeit bzw. Notwendigkeit der medikamentösen Behandlung des Stotterns. [The possibility and necessity of drug treatment of stuttering.] Deutsches Medizinisches Journal, 1962, 13, 467-469.

The author reports his experience with methylpentynol for the treatment of stuttering in approximately 40 patients. The drug is available in 0.25 g capsule form or as drops (30 drops = 1 ml = 0.15 g). Ten patients showed no improvement or retrogressed. Another 12 patients showed partial improvement under treatment which was, for other reasons, suspended before completion. Finally, 15 patients responded favorably. Dosages are stated to be very variable, but are not given except in a few cases. The drug appears highly promising in cases uncomplicated by cerebral disorders.

Poliklinik für Stimm- und Sprachkranke
Freie Universität zu Berlin
Berlin, Germany

1467 Finke, H. Über die Behandlung der Depression mit Nardil (Phenelzin) in der ambulanten Praxis. [Ambulatory treatment of depression with Nardil (phenelzine).] Hippokrates, 1962, 33, 312-316.

Clinical studies
Abstracts 1468-1471

Phenelzine (average 4 tablets/day) was used over a 2 1/2-year period in 72 ambulatory patients falling into 4 groups: endogenous depression; reactive, neurotic depression and collapse conditions with depressive symptomatology; involutional and climacteric depression; and schizophrenia with depressive symptoms. Out of 25 patients in the first group, 15 were cured, 4 greatly improved, and 6 somewhat improved. In the second group, 23 were cured or greatly helped and 7 showed moderate improvement. In the third group, 3 showed no change and 11 either considerable improvement or total cure. In the fourth group (3 patients), there were no cures. Maintenance therapy was given at 1 tablet/day. The only side effects noted were orthostatic hypotension, headaches, dizziness, and respiratory difficulty, all of which could be eliminated by reducing the dosage or, in cases of hypotension, by administration of vasopressor drugs.

Wilhelmstrasse 5
Kassel 35, Germany

1468 Klein, Donald F., & Fink, Max. Behavioral reaction patterns with phenothiazines. *Archives of General Psychiatry*, 1962, 7, 449-459.

Two-hundred-and-seven hospitalized patients received psychotherapy and drugs; chlorpromazine (600-2000 mg/day), promazine (600-1000 mg/day), prochlorperazine (30-90 mg/day) or imipramine [dosage unspecified] were used. Evaluation was made essentially on patterns of changes in 8 target symptoms, i.e., suppressive denial, reduction of anger, affective stability, autistic compliance, decreased agitated depression, somatizing, unaffected episodic agitation, unaffected episodic anxiety and miscellaneous. Improvement was general in all categories except unaffected episodic agitation and anxiety. Extrapyramidal side effects were controlled by trihexyphenidyl, orphenadrine or procyclidine, the latter being favored (dosage 10-15 mg daily). A discussion relating to current psychopharmacological research, patient population descriptions, medication effects, target symptoms

and modes of drug action is also included.

Department of Experimental Psychiatry
Hillside Hospital
Glen Oaks, N. Y.

1469 Carrier, J., Hamoneau, G., Plassat, & Bernes, J. Contribution à l'étude des thérapeutiques antialcooliques. [Contribution to the study of antialcoholic therapies.] *Journal de Médecine de Lyon*, 1962, No. 1008, 647.

A total of 189 treatments was carried out, 145 with apomorphine [no dosage specified] and 43 with disulfiram [dosage unspecified]. On the basis of sobriety for at least a year 10.6% were improved with apomorphine and 37.2% with disulfiram.

Hôpital Psychiatrique de Saint-Jean-de-Dieu
Lyon, France

1470 Broussolle, P., Achaintre, A., Tiebaut, & Barbier. Etudes évolutives et comparatives à l'aide du test de comportements de Fergus Falls. [Developmental and comparative studies on behavior using the Fergus Falls test.] *Journal de Médecine de Lyon*, 1962, No. 1008, 644.

In a brief note, the Fergus Falls test was found to be restricted to banal components of behavior and insufficiently centered on the psychopathology of the subject. A hospitalized group of geriatric patients was studied weekly for several months. The test did allow more objective judgement when coupled with the personal impressions of the therapist.

[No address]

1471 Miribel, J., & Ferreno, E. Le P.M. 671 en dehors du Petit Mal Epileptique. [P.M. 671 aside from petit mal epileptic seizures.] *Journal de Médecine de Lyon*, 1962, No. 1008, 651.

Ethosuximide (P.M. 671) was used in treatment of 80 patients, most with petit mal epilepsy but 10 with other conditions, e.g., Ramsay-Hurt syndrome,

infantile encephalopathies and other conditions with abnormal EEG's. The drug [dosage unspecified] was found as efficacious in these conditions as it is in petit mal epilepsy.

[No address]

1472 Oltman, Jane E., & Friedman, Samuel. Comparison of temporal factors in depressive psychoses treated by EST and antidepressant drugs. *American Journal of Psychiatry*, 1962, 119, 579-580.

A statistical comparison was made between manic-depressive female patients, 119 in the depressive phase who received ECT (EST) for 3 years and 72 comparable patients who received antidepressant drugs for a similar period of time. Follow-up studies were maintained for 2 years. (The 2nd period of study was prorated to equal the initial time span.) A 46% overall rise in hospital admissions accompanied a 37% increase in depressive psychoses. Six percent of the drug-treated patients received some ECT during the initial portion of the study. Patients in the drug group enjoyed a diminished period of hospitalization. With ECT, 60% of the patients were hospitalized for more than 3 months as compared with 31% in the drug group. Individual hospitalization in excess of 6 months totaled 24% with ECT and 10% with drugs. Average length of total hospitalization during the drug era was 37% of that observed during ECT. After 2 years, 20% of the ECT group and 6% of the drug group were still hospitalized. One drug-treated patient committed suicide. Readmissions were slightly in favor of the ECT group.

Fairfield State Hospital
Newtown, Conn.

1473 Thorn, Ingrid. Primidone and chlordiazepoxide in cerebral palsy. *Developmental Medicine and Child Neurology*, 1962, 4, 325-327.

Chlordiazepoxide (0.25-1 mg/kg p.o.) or primidone [dosage unspecified] were administered for 1 month to 1 year to 50 patients

aged 1-15 years with athetosis or quadriplegia due to cerebral palsy. The drugs reduced muscular hypertonicity, improved performance of voluntary movements, partially reduced hyperkinetic movements, diminished sleep disturbance due to muscular activity and crying but exerted no definite effects on emotional reactions. Drug effects were often observable within 24 hours, and were optimal in cases of athetosis or rigidity. Twenty patients responded favorably, 16 moderately, 10 not at all and 4 poorly. Side effects included drowsiness in 23, irritability and depression in 6 and enuresis and encopresis in 1. Individual patients often reacted differently to primidone and to chlordiazepoxide. Combined results were about equally efficacious. Work is contemplated with diazepam. Drug therapy is a valuable adjunct to the standard therapeutic regimen utilized in cerebral palsy.

University Clinic of Pediatrics
Rigshospitalet
Copenhagen, Denmark

1474 Keats, Sidney, Kambin, Parviz, & Nordlund, Thora. Clinical experiences with chlordiazepoxide (Librium) in infantile cerebral palsy. *Developmental Medicine and Child Neurology*, 1962, 4, 336-337.

Chlordiazepoxide (5-40 mg/day p.o.) was administered for 1 1/2 - 7 months to 86 children with cerebral palsy who had undergone treatment for an average of 3 years. Using absences of side-effects and improvement in physical and emotional status as criteria for evaluation, 16 children were rated as good, 25 as fair, 35 without change and 10 as poor. Chlordiazepoxide was tolerated best by spastic cerebral palsy patients. Athetoid and ataxic patients could not tolerate high doses. Emotional status was improved and progress was observed in the physical therapy schedule. A muscle relaxant effect was exerted in the rigidity group. Further studies are indicated, particularly in patients whose progress is hampered by anxiety and tension.

Clinical studies
Abstracts 1475-1478

Cerebral Palsy Treatment Center
New Jersey Orthopedic Hospital
179 Lincoln Avenue
Orange, N. J.

1475 Green, Carl L. Manic depressive psychosis, responded favorably to ECT and medication, particularly chlorpromazine. A 51-year-old male patient evidencing the manic phase of manic depressive psychosis received ECT and tranquilizers [unspecified] which precipitated a return to an apparently normal functional status. Extensive discussion of the case followed presentation of the history.

Louisville General Hospital
Louisville, Ky.

1476 Gruber, Charles M., Jr., & Baptisti, Arthur, Jr. Effectiveness and acceptability of single oral doses of morphine in postpartum patients. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 879.

In a double-blind study, capsules containing placebo or 15-120 mg of morphine were administered to groups of 6-200 postpartum patients after which drug effectiveness, acceptability and safety were determined from 1-6 hours after drug administration. Frequency and intensity of symptoms were also evaluated 6 hours after drug administration. Since changes in pain intensity were directly proportional and relief of pain inversely proportional to the initial pain, drug efficacy comprised a summation of these 2 estimates of analgesia. Thus, the effectiveness/acceptability ratio of dose-response was calculated for morphine. This assay technique will be evaluated by comparing results with those obtained from using n-acymethadol, and experimental drug.

[No address]

1477 Sanger, Maury D. The use of tranquilizers and antidepressants in allergy. *Annals of Allergy*, 1962, 20, 705-709.

After presenting a discussion of the allergic patient, pointing out that he is frequently under both physiological and psychological

stress, the general action of the psychotropic drugs is reviewed. A study in which tranquilizers and/or antidepressants were administered to 186 patients selected from a larger group on the basis of a 2 year study is discussed. These patients had "break-throughs" although suitable antiallergic treatment was used. Tranquilizers including meprobamate, prochlorperazine, perphenazine, chlorthalidone, phenobarbital, etc. (dosages not given) administered to 121 patients produced good to excellent results in 60%. Antidepressants including nialamide, phenelzine, amphetamine, imipramine, and amitriptyline administered to 113 patients (including 48 who did not respond to tranquilizers) produced good to excellent response in 61%. The most frequent side effect was drowsiness with only 1 severe reaction reported in a 6-year-old child who had been given 24 mg doses of perphenazine. Responses to MAO inhibitors was slower with more side effects. Best results were obtained with imipramine and particularly amitriptyline which were effective in 5-7 days. Three case histories are given as illustration.

Veterans Administration
Brooklyn Outpatient Clinic
Brooklyn, N. Y.

1478 Bernstein, Arthur, & Simon, Franklin. Anxiety and angina pectoris. *Angiology*, 1962, 13, 17-22.

The mechanisms of pain in angina mediated through catecholamines and renal pathways are reviewed. Major factors precipitating angina pectoris are physical effort and emotional stress. Management of the former is self-evident and the latter difficult. Emotional factors also present a problem in evaluating the therapeutic efficacy of anti-anginal drugs. Neither supposedly objective tests, double-blind studies, nor "clinical impressions" can be depended upon to give adequate criteria for critical evaluation, and care must be taken to avoid dependence upon any single technique. Experience has shown that papaverine, dioxylone, the nitrates and MAO inhibitors are effective antianginal agents. Their efficacy is considerably enhanced by the addition of a sedative. In this respect, the barbiturates

and tranquilizers have been of great help, but undesirable side effects, particularly oversedation and habituation, limit their usefulness. The authors have used chlor-diazepoxide 5 mg q. i. d in combination with papaverine or dioxylone phosphate in 120 patients with angina for a period of 1-2 years. there has been definite improvement in 90% but reports of drowsiness in 10%. Use of an MAO inhibitor as a single agent in the future shows great promise, as some possible MAO inhibitor mechanisms of action are: coronary dilation through increased 5HT hemic content; blockade of neurohumoral CNS transmission and in sympathetic ganglia; decreased levarterenol sensitivity of the heart, and changes in carbohydrate metabolism.

2130 Millburg Avenue
Maplewood, N. J.

1479 Sumner, David. The treatment of parkinsonism with UK 738: a clinical trial. *American Journal of Psychiatry*, 1962, 119, 534-537.

Twenty patients took part in an open trial with methylbenztropine (UK 738). The dose used ranged from 4-10 mg/day in divided doses. Six mg was found to be the optimal dose. Sixteen of the 20 improved, 1 was unchanged and 3 found intolerant. At this point a double-blind crossover study lasting 3 months was undertaken using 20 patients. Identical tablets contained either 2 mg methylbenztropine, and inert substance or 2.5 mg benzhexol. Methylbenztropine had only a very slight effect on the symptoms of Parkinson's disease and was not as effective as benzhexol. No side effects were seen with benzhexol but 2 patients complained of lightheadedness with methylbenztropine.

Neurological Registrar's Office
General Infirmary
Leeds, Great Britain

1480 Pearse, J. J., & Reiss, Max. Symposium on psychoendocrinology. II. Psychoendocrine aspects of mental retardation. *Canadian Psychiatric Association Journal*, 1963, 8, 14-23.

The relationships between mental and physical retardation were studied in 150 subjects. Most were diagnosed as "undifferentiated" and "familial"; all revealed the following indications of endocrine insufficiency: retardation in growth and weight, thyroid hypofunction, adrenocortical hypofunction and retardation in gonadal development. The patients were approximately 9 to 15 years of age. They were treated with thyroid and/or gonadotropic hormone, e.g., 2-3 grains of dried thyroid daily, 1000-5000 of gonadotropic hormone. In mongoloids, ¹³¹I neck uptake and 24-hour red cell uptake (radioactive triliodothyronine) studies were undertaken. While mongoloids examined showed signs of gonadal underdevelopment, they did not seem to suffer from thyroid deficiencies. Degrees of improvement throughout the caseload were exemplified in 4 case histories, e.g., improvement in behavior and I.Q. in a hypothyroid patient.

Neuro-Endocrine Research Unit
Willowbrook State School
Staten Island 14, N. Y., N. Y.

1481 Woods, Grace E. Preliminary clinical trial of carisoprodol in infantile cerebral palsy. *Developmental Medicine and Child Neurology*, 1962, 4, 28-34.

Forty-six cases of cerebral palsy (9 athetoid, 25 spastic diplegia and 12 various) were treated with carisoprodol, beginning with 250 mg morning and midday. Readings were made by various staff members, e.g., occupational therapists. Marked improvement was noted in 16, some improvement in 17, no improvement in 11 and the condition was worsened in 2. Athetoids showed the most marked degree of improvement and spastic diplegics also showed improvement. Drowsiness was a prevalent side effect. This was considered a serious impediment to learning in these children. Irritability was also common and, in 1 child, controlled with thioridazine. The latter drug was recommended for controlling this side effect.

Hortham Hospital
Almondsbury, Bristol
Great Britain

Clinical studies
Abstracts 1482-1483

1482 Blom, S. Trigeminal neuralgia: its treatment with a new anticonvulsant drug (G-32883). *Lancet*, 1, No. 7234, 839-840.

G-32883 (400-800 mg/day p.o.) was administered to 11 patients with classical trigeminal neuralgia for 6 months. Six patients were symptoms free within 24 hours. Slight numbness remained in 4 patients, and 1 feeble-minded woman was only partially aided by the drug (i.e., her attacks became less frequent). Slight giddiness which subsided in a few days constituted the only side effect in 6, while exanthema developed in 1 patient. Four patients who were previously unresponsive to diphenylhydantoin reacted favorably to G-32883 without the vertigo which had precluded diphenylhydantoin administration. When dosages of G-32883 were lowered or the drug withdrawn, paroxysmal pain returned within 24 hours. No conclusions can be drawn as of yet with respect to long term drug effects. Prior to the advent of G-32883, diphenylhydantoin (300-600 mg/day p.o.) was administered to 22 patients with trigeminal neuralgia for 6 months to 3 years. Operations were performed in 3 cases due to failure of drug treatment or development of intractable side-effects. Freedom from pain prevailed in 8, 9 received considerable amelioration, 1 experienced only slight improvement and 4 were unaffected. Moderate to severe vertigo occurred in 14, necessitating cessation of treatment in 2 (who were vastly improved on G-32883). Two reacted well initially to diphenylhydantoin, but could obtain no real long-term relief until G-32883 was substituted.

Department of Neurology
University Hospital
Uppsala, Sweden

1483 Tortora, Anthony R. Influence of acetophenazine (Tindal) upon the attitude of cardiac patients. *Journal of American Geriatrics Society*, 1962, 10, 270-273.

Fifty heart patients, aged 34 to 86 years, were given acetophenazine (Tindal), 20 mg tablets 2-4 times daily. The diagnoses included 11 hypertensive arteriosclerotic heart disease, 11 arteriosclerotic heart disease, 11 postmyocardial infarction, 2 rheumatic heart disease, 2 coronary insufficiency, 2 essential hypertension, 1 premature ventricular contractions, 1 heart block and 9 cardiac neurosis cases. Nineteen had definite psychoneuroses and 2 Parkinson's disease. A study of 12 angina pectoris patients was also made, and these cases were given a coronary vasodilator for 3 weeks followed by the addition of 20 mg acetophenazine t.i.d. for 4 weeks. Then the vasodilator was replaced with a placebo for 3 more weeks. The degree of frequency of anginal pain was recorded during each of the 3 courses of treatment. There was a definite reduction in the frequency and severity of pain in 7 who were emotionally upset when acetophenazine was added to the regimen. Four patients who had concomitant neoplastic disease needed less analgesics. Improvement in the 50 patient case load was 27 excellent, 17 good and 6 poor. Twelve of the 50 cases showed mild and transient side effects: 4 experienced drowsiness which disappeared with dosage reduction; pruritis was observed in 3 which persisted in 2 despite dosage reduction, and 2 patients complained of mild agitation during the first 4 days of acetophenazine therapy. Further 1 case each of heartburn, headache and dry mouth occurred.

8303 Fourth Avenue
Brooklyn 9, N. Y.

See also 1370, 1375, 1380, 1413, 1498, 1606, 1614, 1651.

SIDE EFFECTS

1484 Jones, E. B., & Williamson, D. A. J. Thalidomide and congenital abnormalities. *Lancet*, 1962, 2, 222. [Letter]

Apparently the recent increase in the incidence of congenital limb defects is due to thalidomide and numerous other nonspecific operant factors, the identity of which are presently unknown. Only 1 history of thalidomide administration in early pregnancy was obtained in 8 instances of birth defects.

Royal Hampshire County Hospital
Winchester, Great Britain

1485 Wroblewski, Felix. Follow up of thioridazine administration. *American Journal of Psychiatry*, 1962, 119, 589. [Letter]

A physician is accused of misrepresentation in a paper entitled "Jaundice follow-up of thioridazine administration" describing subclinical jaundice in a patient with transient minimal elevations in serum bilirubin and serum transaminase activity following administration of thioridazine. Increasing evidence indicates that minimal elevations in serum transaminase concomitant with administration of chemotherapeutic agents may reflect alterations in liver cell permeability or hepatic drug metabolism rather than drug-induced hepatotoxicity. Frequently, continued administration of a drug associated with transient minimal serum transaminase elevation has resulted in a spontaneous return of the serum laboratory test aberrations or hepatotoxic manifestations to normal levels. Drugs should not be classified as hepatotoxic when clinical aspects and liver function tests remain normal.

Memorial Hospital for Cancer and Allied Diseases
New York, N. Y.

1486 Block, Stanley L. Reply to the foregoing. *American Journal of Psychiatry*, 1962, 119, 590. [Letter]

In reply to queries about his previously published article "Jaundice following thioridazine administration", a physician reaffirms that hepatotoxicity may occur from

thioridazine administration, and substantiates this viewpoint with a case history. The transient changes in serum bilirubin and transaminase which began after 9 months of drug administration returned to normal limits upon discontinuation of therapy. The jaundice described was subclinical and classified as such. Despite concomitant metastatic carcinoma, the patient presently remains in good health with no evidence of hepatic malfunction.

[No address]

1487 Luke, Elizabeth. Addiction to mentholated cigarettes. *Lancet*, 1962, 2, 110-111.

A case of a 58-year-old woman, who became addicted to mentholated cigarettes (up to 80 per day), is described. She developed toxic acute psychosis and was hospitalized as an emergency because of bizarre overactivity which became unmanageable. She had gastrointestinal upset with occasional vomiting; she became oversensitive, irritable and quarrelsome. Her speech was slow and slurred and her gait ataxic. Laboratory and other diagnostic studies were negative. When she stopped smoking the mentholated cigarettes, symptoms disappeared; a brief test with 1 grain menthol t. i. d. reproduced the symptoms.

Royal Mental Hospital
Aberdeen, Great Britain

1488 Jacobziner, Harold, & Raybin, Harry W. Accidental chemical poisonings. *New York State Journal of Medicine*, 1962, 62, 550-553.

Two fatalities are presented, 1 due to an overdose of glutethimide (20 g) in a 47-year-old suicidally depressed male and the other due to a ruptured duodenal ulcer complicated by elevated urine and plasma barbiturate levels in an 8-month-old female admitted in coma. A 3rd case was also described; dry-ice dissolved in water ingested by a 3-year-old female produced no untoward effects.

Poison Control Center
The City of New York Department of Health
New York, N. Y.

Side effects
Abstracts 1489-1493

1489 Garretson, Harvey F., Jr., & Moffitt, Ellis M. Imipramine hydrochloride intoxication. *Journal of the American Medical Association*, 1962, 179, 456-458.

Nonfatal imipramine intoxication occurred in a 22-month-old male following ingestion of imipramine (25 mg). Drowsiness was followed by severe continuous convulsions, opisthotonos, profound respiratory depression, circulatory collapse, hypotension unresponsive to vasopressors and cardiac arrhythmias. Therapy consisted of controlling seizures, maintaining respiration and administering fluids. Several cases from the literature were cited, with full elucidation of symptomatology and subsequent treatment.

Mississippi Baptist Hospital
Jackson, Miss.

1490 Baldrige, Eugene T., Miller, Leona V., Haverback, Bernard J., & Brunhes, Shannon. Amine metabolism after an overdose of a monoamine oxidase inhibitor. *New England Journal of Medicine*, 1962, 267, 421-426.

A 30-year-old woman with a manic-depressive psychosis, attempted suicide by ingesting large quantities of MAO inhibitors, i.e., tranylcypromine and isocarboxazid. The induced MAO inhibition caused changes in the levels of pharmacologically active amines and a marked increase in blood serotonin, a slight increase in blood histamine, a marked increase in urinary tryptamine, metanephrine and normetanephrine and a decrease in urinary 5HIAA, indole-3-acetic acid and vanillyl-mandelic acid. The clinical picture, although due to MAO inhibition, could not be related to changes in the level of any single amine. When first seen, the patient was conscious but had gross and uncoordinated movements, incoherent speech and involuntary motions of the jaw and tongue; 6 hours later she became comatose with a temperature of 105°F. She recovered gradually over a 16 day period, after treatment with i.v. fluids, cooling and antibiotics.

Department of Medicine
University of Southern California
Los Angeles, Calif.

1491 Dwyer, Brian, & Gunner, B.W. Phenacetin cyanosis, barbiturate habituation and cardiac arrest. *Medical Journal of Australia*, 1962, 2, 13-14.

A 28-year-old woman with a history of drug habituation (minimal daily requirement: acetylsalicylic acid, 2500 mg; phenacetin, 1000 mg; codeine, 50 mg and caffeine, 250 mg) presented for laparotomy with pronounced cyanosis. Administration of pethidine (100 mg) and scopolamine (0.4 mg) followed by thiopentone (200 mg) and d-tubocurarine (40 mg) resulted in profound cyanosis followed by cardiac arrest. External cardiac massage coupled with a thoracotomy and skillful intubation procedures proved lifesaving. Considerable resistance to d-tubocurarine was also exhibited during 2 subsequent surgical procedures. The patient's initial cyanosis was apparently due to sulf-hemoglobinemia and methemoglobinemia.

Department of Anaesthetics
St. Vincent's Hospital
Sydney, Australia

1492 Speirs, A. L. Thalidomide and congenital abnormalities. *Lancet*, 1962, 2, 303-305.

Eight out of 10 mothers who bore infants with severe limb defects took thalidomide (75-300 mg/day) during the first few weeks of pregnancy. The characteristic series of malformations attributed to thalidomide is elucidated. Other teratogenic drugs were also mentioned.

[No address]

1493 *British Medical Journal*. Goofballs in goal. *British Medical Journal*, 1963, No. 5324, 198.

A prisoner serving a life sentence died from barbiturate poisoning following an overdose of drugs obtained from an unknown source. Prisoners were known to have circulated d-amphetamine capsules ("purple hearts") and phenobarbital capsules ("goofballs") among themselves.

British Medical Association
Tavistock Square
London, Great Britain

1494 British Medical Journal. Ether Sniffing. British Medical Journal, 1963, No. 5324, 198.

A verdict of accidental death was returned at an inquest where a 27-year-old man explained how his 24-year-old wife's death was accidentally caused by ether sniffing. The couple returned home from a drinking bout, and each took a pint bottle of ether to bed. The husband took one sniff and passed out, only to awake the following morning with his wife dead beside him. Both were previously addicted to ether sniffing, and consumed about 1 pint (0.6 l) per day.

British Medical Association
Tavistock Square
London, Great Britain

1495 Dacie, J. V. Haemolytic reaction to drugs. Proceedings of the Royal Society of Medicine, 1962, 55, 28-30.

A case of hemolytic anemia followed nightly administration of 2-3 sleeping pills containing 3 1/2 g of phenacetin for 2 months. Drug withdrawal preceded rapid return to normality. A 38-year-old woman experienced jaundice and oliguria secondary to hemolytic anemia after taking phenacetin for several months. Phenacetin produced hemolytic anemia in normal therapeutic dosages in normal subjects, in small dosages in glucose-6-phosphate dehydrogenase deficient subjects, and rarely by an auto-immune mechanism. Hemolytic anemias have been attributed to the following drugs: antipyretics and sedatives, sulphonamides, antileprotics, antimalarials, anticonvulsants, urinary antiseptics, antihistamines, antihelminthics and miscellaneous drugs (chlorpromazine, chloramphenicol, etc.). Drug-induced hemolytic anemia occurs by regular mechanisms or is precipitated by some individual idiosyncrasy or hypersensitivity. Racial susceptibility to drugs is predicated on the existence of a deficiency in erythrocytic glucose-6-phosphate dehydrogenase, in not only Negroes, but also Sephardic Jews and certain Mediterranean peoples.

[No address]

1496 Rosen, Carl S., & Lechner, Michael. Jimson-weed intoxication. New England Journal of Medicine, 1962, 267, 448-450.

Two cases of Jimson weed (*Datura stramonium*) intoxication are described. All parts of this plant contain belladonna alkaloids (hyoscyamine, atropine, scopolamine and hyoscyne). In 1 case, a 3-year old boy, symptoms were noted 2-3 hours after ingestion of the seeds; in another case, his 6-year-old sister, 5-6 hours elapsed before symptoms appeared. The boy became markedly confused, disoriented, feverish, displayed muscular incoordination and had convulsions. The girl displayed similar symptoms, except for the absence of convulsions. Treatment was by alcohol sponging and amobarbital [dose unspecified] in the 1st case and by gastric lavage, sodium phosphate and amobarbital in the girl. Both children recovered in 8-12 hours.

Grasslands Hospital
Valhalla, N. Y.

1497 Jacobs, Lionel A., & Morris, John G. Renal papillary necrosis and the abuse of phenacetin. Medical Journal of Australia, 1962, 2, 531-538.

Fifty deceased persons 23-75 years old), 3.7% of those autopsied during 1959-1962 at this hospital, had macroscopic renal papillary necrosis. These cases were analyzed in considerable detail and questionnaires sent to relatives or friends. Forty-seven of these people had been in the habit of taking phenacetin preparations daily and 60% consumed large quantities of phenacetin-containing analgesics for a long period of time before the onset of symptoms of renal disease. Nearly all these people had suffered from marked urinary infections; diabetes mellitus and obstructive uropathies were of minor significance. On final admission, nearly all showed many urinary leukocytes; only 4 persons had a specific gravity above 1.014; the BUN was high in 43 out of 44 and hemoglobin was less than 10 g in 34 out of 46. Diagnosis of such renal disease depends largely on radiological changes and the passing of papillary fragments in the urine for confirmation; a history of phenacetin abuse is also significant. The role of phenacetin in

Side effects
Abstracts 1498-1501

causing chronic interstitial nephritis is discussed; three case histories are given as examples.

Prince Henry Hospital
Sydney, Australia

1498 Morgenstern, G.F. Trihexyphenidyl (Artane) intoxication due to overdosage with suicidal intent. Canadian Medical Association Journal, 1962, 87, 79-81.

A case of trihexyphenidyl intoxication, due to overdosage (180 mg) with suicidal intent, is described in a 29-year-old chronic hebephrenic schizophrenic male, with a history of 4 hospital admissions since the age of 17. He had previously responded well to 200 mg chlorpromazine and 2 mg trihexyphenidyl, each t.i.d. The patient was stuporous upon admission with a fever of 101°F. and respiration somewhat deeper than normal; the skin was dry, flushed and contained liquid blebs. Urinary incontinence was also noted. Treatment was symptomatic, i.e., fluids, aspirin, alcohol sponge, chloramphenicol and penicillin. The intoxication cleared in 5-6 days. Chlorpromazine (300 mg t.i.d.) and trihexyphenidyl (2 mg t.i.d.) were then resumed. Generally, symptoms of this intoxication resembled those of atropine and responded to similar treatment.

Verdun Protestant Hospital
6875 LaSalle Blvd.
Verdun, Quebec
Canada

1499 Mitchell, Hugh G. Chlorpromazine ("Largactil") sensitivity simulating the "acute abdomen." Medical Journal of Australia, 1962, 2, 930. [Letter]

The author describes his own experience with vomiting caused by chlorpromazine [dose unspecified]. He had returned from the Far East with a series of intermittent fevers of unknown etiology. Following attacks of acute pulmonary edema, he was treated with antibiotics, digitalis, acetazolamide and chlorpromazine. He vomited several times a day for months, suffering marked weight loss, in spite of increased doses of chlorpromazine. Contrary to med-

ical advice, he ceased taking medication and vomiting stopped. Vomiting recurred briefly only during the few days when chlorpromazine was resumed.

375 Toorak Road
South Yarra, Vic.
Australia

1500 Greene, Bernard L., Liebman, S., & Lustig, Noel. Dangers of using glutethimide: addiction qualities, symptoms of intoxication, and withdrawal convulsions. Illinois Medical Journal, 1962, 121, 139-141.

Glutethimide, ordinarily thought of as innocuous, can be habit-forming and dangerous. Addiction, signs of chronic anxiety and acute withdrawal convulsions have occurred. A 30-year-old woman had been taking this drug for about 3 1/2 years [dose unspecified] before her hospitalization. Neurotic complaints, marital disharmony, occasionally incoherent speech and falling occurred. Hospitalization was advised but refused. Hospitalization was finally required on an emergency basis as a result of acute withdrawal convulsions and related symptoms. Treatment consisted of glutethimide (1 g q.i.d.), dilantin (1 1/2 g t.i.d.) and multiple vitamins (p.o. and parenterally). The glutethimide was gradually eliminated over 8 days and the patient was discharged on the 11th day. It was recommended that prescriptions containing glutethimide be marked "not to be refilled."

[No address]

1501 Im Obersteg, J., & Bäumler, J. Suicid mit dem Psychopharmakon Tofranil. [Suicide by means of Tofranil.] Archiv für Toxikologie, 1962, 19, 339-344.

A 28-year-old mother with endogenous depression committed suicide by swallowing 5000 mg of imipramine (Tofranil). The similarity in structure and physicochemical properties between imipramine and the phenothiazine derivatives is pointed out and the chromatographic and spectrographic properties of imipramine and its metabolites are presented in tabular form. Whereas in normal usage only its metabolites will be found in the urine, it was possible in this

case to demonstrate the presence of unmetabolized imipramine in the blood, urine and organs. Attention is called to the dangers attending the ambulatory use of this drug, since suicide attempts occur in surprising numbers at the point where, while the psychomotor inhibitions are relaxed, the basic endogenous depression still persists.

Gerichtlich-Medizinisches Institut
Universität Basel
Basel, Switzerland

1502 Matiar-Vahar, H., & Schilde, P. Zerebrale Krampfanfälle bei Glutethimid-Abusus. [Cerebral convulsions due to glutethimide abuse.] Deutsche Medizinische Wochenschrift, 1962, 87, 406-408.

After a review of the literature on glutethimide abuse, the authors present 3 cases of their own, 2 male students both 30 years old, and one 45-year-old woman teacher. The first experienced attacks after a continued ingestion of 8 tablets daily, these consisting of loss of consciousness, rigidity, muscular tremors, and frothing at the mouth. Reports on the 3rd case were somewhat more vaguely reported to the physicians but consisted essentially of several attacks similar to those described above. EEG's taken immediately after the attacks showed alpha-type waves and involutional dysrhythmia. Subsequent EEG's were normal, after use of the drug had been stopped. Caution in the use of the drug, as well as placing the drug under the control of doctors, is recommended.

Psychiatrische und Nervenlinik der
Friedrich-Wilhelm Universität
Kaiser-Karl-Ring 20
Bonn, Germany

1503 von Dittrich, P. Die Behandlung der akuten Vergiftung mit Glutethimid (Doriden) durch extrakorporale Hämodialyse. [Treatment of acute glutethimide intoxication by means of extracorporeal dialysis.] Deutsche Medizinische Wochenschrift, 1962, 87, 357-359.

A 19-year-old male attempted suicide by

ingesting 40 tablets (10 g) of glutethimide. After 3 days of conservative treatment during which no improvement took place, extracorporeal dialysis was resorted to. In 8 hours the patient recovered consciousness, with normalization of reflexes, blood pressure, pulse and respiration. Anuria set in 2 days later, and after 4 days, extracorporeal dialysis was again found necessary. Follow-up 10 weeks later showed normal findings except for some limitation of tubular function and normochromic anemia. The authors discuss the triggering mechanism of kidney failure.

Medizinische Universitätsklinik
Allgemeines Krankenhaus
Innsbruck, Austria

1504 Langecker, H., Neuhaus, G., Ibe, K., & Kessel, M. Ein Suicid-Versuch mit Valamin mit einem Beitrag zur Elimination und Therapie. [A suicide attempt by means of Valamin and a contribution to its elimination and therapy.] Archiv für Toxikologie, 1962, 19, 293-301.

The authors report the case of a 21-year-old man who first attempted suicide with a combination of hypnotics, sedatives, and alcohol. A few days later he again attempted suicide by means of 40 g of ethinamate (Valamin) in combination with Coca-cola and alcohol. About 16 hours later he was admitted showing severe intoxication, spontaneous hypothermia of 28.8°C and severe respiratory insufficiency. Treatment consisted of artificial respiration, leventerenol, extracorporeal dialysis, and suxamethonium. The patient was unconscious for 4 days and then recovered. Chromatographic tests were run on the blood plasma, dialysate, and urine. The methodology is described, and detailed results are presented in chart form. The narcotic limiting concentration in the blood, 17 hours after intake, was about 4 mg%. The presence of 10% metabolites in the urine after 17 hours indicates the great importance of hydroxylation and conjugation in relation to the concentration of urinary metabolites. Extracorporeal dialysis is superfluous in cases of ethinamate poisoning when kidney function is intact.

Hauptlaboratorium Schering AG
Berlin, Germany

1505 Grahmann, Hans, & Peters, Uwe H. Über psychotische Erscheinungen bei INH-Entziehung. [Psychotic manifestations after INH-withdrawal.] Archiv für Psychiatrie und Zeitschrift für die Gesamte Neurologie, 1962, 203, 173-177.

A 62-year-old tuberculosis patient arbitrarily suspended treatment with isoniazid (INH) and developed withdrawal symptoms consisting first of insomnia, then extreme vivacity, incessant inconsequent chattering, wild gesticulations, unproductive talk, and evident pressure of a desire, but also inability, to communicate something important to him. There was no clouding of consciousness. The full development of the symptoms took place over a 2-day period, and lasted for about 1 day, with subsequent recovery.

Psychiatrische und Nervenlinik
Universität Kiel
Kiel, Germany

1506 Cramer, Hinrich, & Binet, Jacques-Louis. B₆-Avitaminose und Nervensystem. [B₆-avitaminosis and the nervous system.] Ärztliche-Forschung, 1962, 16, 53-59.

A 61-year-old female tuberculosis patient developed cerebral complications due to vitamin B₆ deficiency following treatment with isoniazid. These consisted of an epileptic-type seizure, followed by severe headaches. Investigation disclosed a disturbance of tryptophane metabolism of the kind described for vitamin B₆ deficiency. Addition of pyridoxine to the treatment over a 3-week period resulted in normal tryptophane metabolism, while the sputum examination remained negative, thus indicating that pyridoxine does not interfere with the antituberculosis effects of isoniazid.

Clinique des Maladies du Système Nerveux
Hôpital de la Salpêtrière
Paris, France

1507 Sours, John A. Peripheral edema and tachycardia during tranlycypromine therapy. American Journal of Psychiatry, 1962, 119, 584-585.

Following administration of chlorpromazine (50-75 mg q. i. d.) and tranlycypromine (10 mg q. i. d.) for 10 days, a 28-year-old male acute schizophrenic with secondary gastrointestinal psychophysiological complications manifested sinus tachycardia and 2+ edema of the ankles, right knee and wrist. Discontinuation of tranlycypromine resulted in dramatic disappearance of symptoms within 24 hours. This constituted the first recorded case of tranlycypromine induced edema and tachycardia occurring simultaneously in a given individual. Drug-induced side effects are directly related to dosage, and quantities in excess of 30 mg q. i. d. increase both the incidence and severity of side effects.

Department of Psychiatry
U.S. Naval School of Aviation Medicine
Pensacola, Fla.

1508 Bacon, G.A. Successful suicide with tranlycypromine sulfate. American Journal of Psychiatry, 1962, 119, 585.

A 17-year-old female received a prescription for tranlycypromine (50- 10 mg tablets) to combat a neurotic depressive reaction. She immediately proceeded to ingest all 50 tablets. Within 2 hours, she became agitated, incoherent and markedly tremulous. Phenobarbital (1 grain i. m.) and secobarbital (2 grains i. m.) were administered over a 4 hour period following hospital admission. (The attending physician was unaware of the number of tablets taken). The patient became comatose and critically ill, with hyperthermia (110°F) and circulatory collapse. Intranasal O₂ and levarterenol bitartrate (3 ampules in 5% glucose over 3 hours), plasma, hydrotherapy and gastric lavage were unable to prevent death from ensuing within 8 hours of drug ingestion. Due to a technical error, gastric lavage was postponed for 5 hours after tablets were taken. Death was essentially an exaggeration of the side effects, which normally occur with tranlycypromine in standard and intensive treatment dosages.

St. Luke's Hospital
Racine, Wisc.

1509 French Devitt, R.E., & Kenny, Sheila. *Lancet*, 1962, 2, 430. [Letter]

Within an 8-month period, 3 cases of phocomelia due to thalidomide were observed in an area with an 8-year birth record unmarked by a single case of phocomelia. Of these 3 patients, 1 received an unknown amount of thalidomide throughout pregnancy and 2 received 100 mg/day from the 5th to the 11th or 13th week of pregnancy.

South Down Hospital Group
Newry, County Down
Ireland

1510 Calnan, C.D. Contact dermatitis from drugs. *Proceedings of the Royal Society of Medicine*, 1962, 55, 39-42.

The author lists 772 cases of contact dermatitis caused by the following compounds: antibacterial agents - 220, antibiotics - 124, local anesthetics - 74, antihistamines - 53, colophony resin - 14, rubefacients, - 8, miscellaneous - 88, all of which are allergic reactions; he includes cases caused by occupational contacts: chlorpromazine - 175 and antibiotics - 16. Antibiotics, local anesthetics and antihistamines are the major topical sensitizers. Patch test concentrations, differences among countries, trends in sensitization, e.g., neomycin sensitivity is steadily increasing with its extending usage and some effects of legislation are reviewed. Phenothiazine derivatives (particularly promethazine and chlorpromazine) have become prominent in photocontact dermatitis. The best way to reduce the incidence of reactions is to use minimal effective concentration for minimal periods of time.

[No address]

1511 Chapman, John E., & Lewis, Charles E. Darvon, Dieldrin and Noludar. *Journal of the Kansas Medical Society*, 1962, 63, 228-229.

A 63-year-old woman ingested 780 mg of dextro propoxyphene hydrochloride (Darvon) and was admitted with severe hypotension and dangerously diminished respiratory

rate. Intubation and artificial respiration precipitated a full return to consciousness within 18 hours of poisoning. Overdoses of Darvon lead to CNS depression. The concomitant respiratory depression may be alleviated by nalorphine. A 47-year-old female ingested 4-5 ounces of insecticide containing dieldrin, followed by 2-3 ounces of household ammonia, after which she vomited and experienced 13 grand mal seizures, which were controlled by i.m. and i.v. administration of barbiturates administered following gastric lavage. A 26-year-old colored female took 2700 mg of Noludar (3,3-diethyl-5-methyl-2,4-piperidinedione) and promptly became semicomatose. Gastric lavage within 1 hour after drug ingestion was followed by an uneventful recovery. Psychiatric help was proffered. Cardiovascular and respiratory support constituted adequate treatment in all cases. The Poison Control Center cases illustrate the need for rapid evaluation and treatment of patients suffering from an overdose of poisons common to most households.

Department of Pharmacology
University of Kansas Medical Center
Kansas City, Kan.

1512 McCawley, Elton L., Brummett, Robert E., & Dana, George W. Convulsions from psilocybe mushroom poisoning. *Proceedings of the Western Pharmacology Society*, 1962, 5, 27-34.

Six cases of mushroom poisoning are reported. There were 2 adults and 4 children, aged 4-9 years. Within 15-30 minutes after eating the cooked mushrooms, the adults reported a sense of anxiety and excitement described as a "cheap drunk." The children were reported variously to emit a peculiar cry, be dizzy and ataxic, were weak, disoriented, staring or incoherent. All exhibited mydriasis with the pupils widely dilated and fixed. When tested, however, the pupils responded to light and accommodation. The mouth was dry, the skin dry and flushed although some patients reported a feeling of being cold. All complained of nausea and stomach cramps. All the children developed clonic-tonic type convulsions which were usually

Side effects
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intermittent. One child died. Species identification was possible in 1 case, the mushroom being *Psilocybe baeocystis*. Paper chromatography was used on a sample and psilocybin identified as the major component with lesser amounts of psilocin present.

Department of Pharmacology
University of Oregon Medical School
Portland, Ore.

1513 Jacobziner, Harold, & Raybin, Harry W. Mixture of tranquilizers, lighter fluid, paint thinner, and iodine poisonings. *New York State Journal of Medicine*, 1962, 62, 862-864.

Four cases of accidental poisoning included a 21-month-old male who ingested charcoal lighter fluid, a 2-year-old male who swallowed paint thinner, an 11-year-old girl who gargled with an iodine solution, and a 34-year-old female schizoaffective schizophrenic who probably ingested unknown amounts of the following psychoactive drugs: trifluoperazine, imipramine, meprobamate and promazine along with iodine. Marked cerebral depression was evident upon admission, and the initial stupor rapidly progressed to profound coma. Treatment entailed gastric lavage, metaraminol bitartrate infusion and intubation. Rapid recovery ensued. Subsequent psychiatric care included 8 ECT treatments with concomitant psychotherapy.

Poison Control Center
The City of New York Department of Health
New York, N. Y.

1514 Jacobziner, Harold, & Raybin, Harry W. Glutethimide (Doriden) poisoning. *Archives of Pediatrics*, 1962, 79, 302-305.

Glutethimide poisoning occurred in 62 individuals, aged 2-70 years, with only 1 fatality (a 64-year-old male who ingested 6 g in a suicidal attempt). Prominent features of acute poisoning include drowsiness, nausea and vomiting, which precede cerebral edema, hypotension and circulatory

collapse. Supportive symptomatic treatment encompasses gastric lavage, fluids, chlorpromazine, caffeine and intubation procedures. A heroin addict who attempted drug withdrawal by ingesting glutethimide (15 0.5 g tablets/day) took an overdose of 12 g in 48 hours and awoke in Bellevue with no ill effects. A complete subjective history of glutethimide addiction was described in a 25-year-old man. Ingestion of more than 1-1/2 g to combat depression resulted in amnesia, a transient psychotic reaction and profound sleep. Drug discontinuation precipitated withdrawal symptoms, including impaired voluntary muscle coordination, general trembling and gastric distress. Toxic reactions attributed to glutethimide mimic those obtained from the barbiturates.

125 Worth Street
New York 13, N. Y.

1515 Smithells, R. W., & Lond, M. G. Thalidomide and malformations in Liverpool. *Lancet*, 1962, No. 7242, 1270-1273

Fifty-nine mothers gave birth to malformed babies in Liverpool since January 1, 1960. Of the women who had 30 babies evincing ectomelia (gross hypoplasia or aplasia of 1 or more long bones or limbs, including amelia, phocomelia and hemimelia), 12 ingested thalidomide in the 1st trimester of pregnancy. Seven infants had microtia (gross hypoplasia or aplasia of the pinna with or without external auditory meatus) and 3 of their mothers took thalidomide, but thalidomide was ingested by only 2 mothers in a series of 22 infants born with lesser deformities. A group of 40 healthy infants acted as controls. Liverpool instituted a congenital abnormalities registry to facilitate repercussions arising from the thalidomide tragedy. Personal interviews with involved persons indicated the fallibility of retrospective data in attempting to designate which drugs were ingested and dosages of same. Of the 30 babies with ectomelia 11 were still-born, males outnumbered females by 2 to 1, and associated malformations were observed in 12. Other drugs ingested concomitantly with thalidomide include barbiturates,

glutethimide and antiemetics. Six mothers of ectromelic infants had clinical influenza and 1 had encephalitis during the 1st trimester of pregnancy. The fact that a history of thalidomide ingestion was obtained from less than half of these mothers may be a reflection of the fallibility of memory and records, or malformations may be virus-induced or precipitated by other drugs with unsuspected teratogenicity. Thalidomide has been responsible for a minimum of 800 fetal malformations in Great Britain

[No address]

1516 Dally, P. J. Fatal reaction associated with tranlylcypromine and methylamphetamine. *Lancet*, 1962, No. 7241, 1235-1236.

A 38-year-old man received methamphetamine [dosage unspecified], and immediately experienced severe hypertension and an excruciating occipital headache. Aspirin and amylobarbitol [i.v.] provided relief fairly rapidly. Intravenous methamphetamine administered to patients concomitantly or within 2 weeks of MAO inhibitors (iproniazid, phenelzine, isocarboxazid, phenoxypropazine, pheniprazine, nialamide or tranlylcypromine) may result in rapid development of severe occipital headache, chest constriction, tachycardia, palpitations, increased respiratory rate and vomiting. Similar symptoms occur with long-term administration of MAO inhibitors. As such side effects resemble hypertensive paroxysms associated with pheochromocytoma, (thus implicating the adrenal medulla in etiology) the hypertensive crisis may respond favorably to a sustained-action catecholamine inhibitor like dibenamine.

Department of Psychological Medicine
Westminster Hospital
London, S.W. 1, Great Britain

1517 Dubach, U.C. Methyldopa and depression. *British Medical Journal*, 1963, No. 5325, 261.

A patient with carcinoid syndrome received α -methyldopa (2-2.5 g/day) to control carcinoid flushes. The medication neither controlled diarrhea nor altered blood pressure. The patient evinced marked slowing of motor activity and psychic hallucinations which subsided 24 hours after drug withdrawal. Another patient with carcinoid syndrome also received α -methyldopa (1 g/day) and showed a markedly increased sleeping tendency with some motor retardation during the period of drug administration. Reversal of symptoms has been the rule upon drug withdrawal.

Medizinische Universitätspoliklinik
Basel, Switzerland

1518 Kirman, Brian H. "Ancoloxin" and foetal abnormalities. *British Medical Journal*, 1963, No. 5325, 265-266.

Ancoloxin (meclozine and pyridoxine) administered to pregnant women 7 1/2-10 weeks after the last menstrual period may, contrary to popular opinion, cause meningocele in the embryo despite the fact that the neural tube closes by the 6th week of gestation, since the excessive variation in ovulation enables fertilization to occur at any time during the cycle. Adequate investigation should be undertaken by scientists who are not affiliated with pharmaceutical companies or financially dependent upon them. Such conditions would indubitably enhance objective interpretation of data.

Carshalton, Surrey
Great Britain

1519 McClure, J. L. Reactions associated with tranlylcypromine. *Lancet*, 1962, No. 7243, 1351.

Tranlylcypromine (20-40 mg/day) administered to 3 patients, aged 18-36 years for 5 days to 4 weeks resulted in palpitations, severe occipital headache, vomiting, profuse sweating, hypertension and photophobia. Drug withdrawal resulted in cessation of symptoms within 12-48 hours in 2 patients, but the 3rd died 4 1/2 hours after the onset of symptoms from a ruptured aneurysm of the left posterior

communicating artery.

Maudsley Hospital
London, S.E. 5, Great Britain

1520 Mason, Alan. Fatal reaction associated with tranlycypromine and methylamphetamine. *Lancet*, 1962, No. 7238, 1073.

A 39-year-old man was previously treated for depression with hysteria by ether inhalation and 25 mg i.v. methylamphetamine on 3 occasions. Hysteria was obliterated and tension was reduced by this means. During a 3-week interval, tranlycypromine (10 mg t.i.d. for 2 weeks) was administered, followed by a 25 mg injection of methylamphetamine, which precipitated a severe headache followed by a left hemiparesis (with blood CSF) that culminated before death due to a massive cerebrovascular accident. Autopsy revealed a predisposition to vascular difficulty in the form of considerable atheromatous degeneration of cerebral arteries, which could have reacted similarly to methylamphetamine or tranlycypromine. Timing, however, indicated that death was due to the effects derived from a combination of the 2 drugs.

[No address]

1521 Stark, D. C. C. Effects of giving vasopressors to patients on monoamine-oxidase inhibitors. *Lancet*, 1962, No. 7244, 1405-1406.

A 33-year-old woman with anxiety received chlordiazepoxide and phenelzine [dosages unspecified] for 1 month prior to bilateral angiography to determine the origin of recurrent headaches. (family history included loss of 3 sisters from subarachnoid hemorrhages due to ruptured aneurysms of the circle of Willis.) Premedication included pethidine (50 mg) and atropine (0.65 mg). Anesthesia included thiopentone (300 mg), suxamethonium (50 mg), and 1% halothane, etc. Hypotension followed manipulation of the left carotid artery, and mephentermine (10 mg i.v.) was administered to facilitate puncture. Gross tachycardia and hypertension ensued immediately, but rapid administration of

oxygen precipitated a return to normal levels within 15 minutes. A hematoma of the right carotid sheath developed simultaneously with the hypertension and angiography was abandoned. Recovery was uneventful. Effects were apparently due to the combination of a sympathetic amine with a MAO inhibitor, a combination which has proved to be catastrophic at best.

Newcastle General Hospital
Newcastle-upon-Tyne, Great Britain

1522 Quibell, E. P. Thalidomide-damaged infants. *Lancet*, 1962, No. 7244, 1402.

Effective aid must be provided for a possible total of 500 thalidomide damaged babies in Great Britain (11 of which occurred in a single practice). Difficult individual problems may be partially ameliorated through an initial pediatric assessment to evaluate the problem and ascertain associated defects, early reference (6-8 weeks of age) to a limb-fitting surgeon and early consultation with an orthopedic surgeon. All efforts should be directed toward obtaining an effective functional result. Special prosthetic equipment is indicated and should be instituted as early as possible, in conjunction with the development of understanding parental attitudes. Long range goals should revolve around enabling such children to achieve a reasonable degree of independence since their level of intelligence is essentially unimpaired. Parental attitudes are of the utmost importance and must be sympathetic and understanding at all costs. Coordinated medical endeavors offer the most promising solution to the thalidomide problem.

Chailey Heritage
Craft School and Hospital
Chailey, Sussex
Great Britain

See also 1372, 1373, 1378, 1382, 1384, 1386, 1390, 1391, 1392, 1405, 1407, 1409, 1419, 1420, 1421, 1429, 1446, 1585, 1648, 1649.

1523 Posner, Herbert S., Hearst, Eliot, Taylor, Wilson L., & Cosmides, George J. Model metabolites of chlorpromazine and promazine: relative activities in some pharmacological and behavioral tests. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 84-90.

NIH general purpose male mice were used in the sleeping time and rotating rod tests, and male Wistar or Osborne-Mendel rats were used in operant behavior tests. The effects of chlorpromazine, chlorpromazine sulfoxide, monomethylchlorpromazine, chlorpromazine-N-oxide, promazine, 2-hydroxypropazine, and 4-hydroxypropazine were studied in relation to potentiation of hexobarbital sleeping time, on stimulated locomotor activity (rotarod test, Kinnard and Carr 1957) and on CR's. In all tests, chlorpromazine sulfoxide was the least active, chlorpromazine-N-oxide though active was less active than chlorpromazine or monomethylchlorpromazine. A lag in the onset of activity was only noted with chlorpromazine-N-oxide in both of the CR tests. Monomethylchlorpromazine was generally only slightly less active than chlorpromazine. 4-Hydroxypropazine was equally or slightly less active than promazine and 2-hydroxypropazine was markedly less active than promazine, except in the sleeping time test when given i.v. In this case it was about as active as promazine, which in turn was less active than chlorpromazine in all tests.

Clinical Neuropharmacology Research Center
NIH
Bethesda, Md.

1524 Hurst, Paul M. The effects of d-amphetamine on risk taking. *Psychopharmacologia*, 1962, 3, 283-290.

The effect of d-amphetamine (10 mg p.o.) on the risk-taking behavior of 29 male prisoners (IQ 104-131; various ages) was investigated, utilizing a gambling situation involving cigarettes. Capsules were ingested 1 1/2 hours before testing. Subjects served as their own controls when receiving placebos. The comparison was done with Wilcoxon's matched pairs rank test to determine the significance of differences between paired observations. The difference was signifi-

cant in the direction of increased risk-taking under the drug; 19 subjects made more high-risk choices while under the drug and 7 while receiving the placebo, while 3 showed no differences. Apparently d-amphetamine can increase risk-taking. Alternative interpretations were also provided.

The Institute for Research
State College, Pa.

1525 Froelich, Robert E., & Heckel, Robert V. The psychological effects of methylphenidate. *Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology*, 1962, 23, 91-98.

Experiments were performed on 90 medical students, in order to study the psycho-effects of methylphenidate. Groups of 5-10 subjects were tested in 2 hourly sessions at 24 hour intervals in 9 experimental categories based on 3 variables. Subjects received methylphenidate (20 mg i.v.), drug being used but not of the dosage or the test design. Evaluation was based on learning, recall and relearning of nonsense syllables, performance of motor tasks (Purdue Pegboard) and writing of imaginative responses (Heckel-Steele Sexual Situations Test). The drug had no significant effect on learning, slightly delayed initial learning and augmented facilitation of recall, tended to produce maximum and superior motor performance on the 1st trial and maintained this performance on the 2nd trial. Imaginative productions under influence of the methylphenidate showed decreased inhibition, increased verbal productivity and expression of previously repressed, emotionally charged feelings. Only 1 out of 51 drug-treated subjects withdrew because of side effects (essentially extreme confusion). There was some difficulty in concentrating and mild exhaustion was observed in most subjects, elevation in pulse rate and anxiety level was noted among both treated and placebo subjects.

University of Missouri School of Medicine
Columbia, Mo.

1526 Knight, David A. Problems of non-specific factors in psychopharmacology. Methodology. Test score instability. A source of error in individual drug response. In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 99-113.

Eighteen normal subjects, aged 20-38 years, were tested on 10 successive occasions with the following tests: Flicker Fusion, After-Image Disappearance, Auditory Reaction Time and Tapping Speed. Nine were tested at fixed hours and 9 at randomly varied hours. Fixed and variable scheduling data were pooled for a 2 way analysis of variance. Individual mean discrepancies were significant at the 0.01 probability level, indicating the heterogeneity of the sample.

Verdun Protestant Hospital
Verdun, Quebec
Canada

1527 Miller, James G. Objective measurements of the effects of drugs on driver behavior. *Journal of the American Medical Association*, 1962, 179, 940-943.

Various combinations of patients and normal subjects received meprobamate (800-1600 mg/day), d-amphetamine, alcohol, prochlorperazine (20 mg), benactyzine, emprocamate (400-800mg), carisoprodol (2100 mg/day), chlordiazepoxide, mebutamate (300 mg), phenobarbital, carbethoxysyngoyl methylreserpate and isothipendyl in order to measure the potentially deleterious effects these drugs have on normal reaction time and judgement as determined by the driver trainer test (American Automobile Association's Auto Trainer), the Whipple Steadiness Test and standard Ortho-rater testing procedures. Most of the tranquilizers did not appear to exert serious behavioral toxicity. Chlordiazepoxide produced diminished accuracy in judgement, some degree of exophoria, and significantly decreased visual acuity. Normal doses of these compounds failed to produce significant behavioral aberrations.

Mental Health Research Institute
University of Michigan
Ann Arbor, Mich.

1528 Thompson, Travis. The effect of two phenothiazines and a barbiturate on extinction-induced rate increase of a free operant. *Journal of Comparative and Physiological Psychology*, 1962, 55, 714-718.

Phenobarbital (30-120 mg/kg i.p.), thioridazine and chlorpromazine (each 0.75-20.0 mg/kg i.p.) were administered to 9 experimentally naive male Sprague-Dawley rats 30 minutes before they were placed in Skinner boxes, drug effects were determined on the rate of lever pressing for water reinforcement on a regular reinforcement schedule. Dose-response-rate curves indicated that a reduction in lever pressing was produced by successive increments of phenobarbital, chlorpromazine and thioridazine. A 2nd group of 27 rats (experimental conditions same as above) in a 3 x 3 factorial design with triple replication per cell received drugs as above to determine the effects of drug and dosage variation on the extinction inflection ratio (EIR), depression of lever-pressing, and degree of ataxia (rearings, inclined-plane behavior, narrow-walkway behavior, and walking in short alley). Overall analysis of variance yielded a statistically significant F ratio which was attributable to a significant dose effect ($p < .01$), with drug and interaction effects failing to reach significance. An inverse relationship was observed between drug dose and EIR magnitude. Subcomparisons indicated that the difference in drug effects was a reflection of phenobarbital deviation from the phenothiazine group. Ataxia scores for the phenobarbital group were significantly higher than those obtained by the 2 phenothiazines, and were directly related to dosage. No interaction effects were observed in the total ataxia scores, and drug effect was contributed solely by the phenobarbital group. No basic difference was indicated in the effect of the 3 drugs on the EIR increase but the effect on ataxic score was significant.

Laboratory of Psychopharmacology
University of Maryland
College Park, Md.

1529 Bures, J., Bohdanecký Z., & Weiss, T. Physostigmine induced hippocampal theta activity and learning in rats. *Psychopharmacologia*, 1962, 3, 254-263.

The effect of physostigmine on EEG activity and conditioning was studied in Wistar rats 2-3 months old. Theta activity, which corresponded to the impairment of learning, developed in the hippocampus of curarized or freely-moving, unanesthetized animals 30-60 minutes after 1 mg/kg i.p., with maximum after 10 minutes. A 1-trial acquisition of a passive avoidance reaction in an electrified compartment was suppressed 10 minutes after 0.2-1.0 mg/kg physostigmine. No retention of this reaction was found 24 hours after 1-trial learning when 0.5 mg/kg was applied 8 minutes before the retention test; this same dose did not impair the retention of an overtrained (4 times) passive avoidance reaction. An overlearned active avoidance reaction (running to the safe part of the apparatus) was not affected by 0.5 mg/kg of the agent and only partly impaired by 1.0 mg/kg.

Institute of Physiology
Czechoslovak Academy of Sciences
Prague, Czechoslovakia

1530 Kornetsky, Conan, Dawson, Joy, & Pelikan, Edward. A hypothesis based on animal experimentation. Individual animal variation in the effects of pentobarbital and dextro-amphetamine (A comparison). In: Rinkel, Max [Ed.] Specific and non-specific factors in psychopharmacology. New York: Philosophical Library, 1962, 161-171.

Nine male Wistar rats were trained in lever-pressing for food reward (50 presses/reinforcement) in a standard Garson-Stadler box. All drugs were administered in aqueous solution i.p. in the following order: day 1, 5.0 mg/kg pentobarbital; day 2, 5.0 mg/kg pentobarbital; day 3, water; day 4, 10.0 mg/kg pentobarbital; day 5, 10.0 mg/kg pentobarbital; day 6, water; day 7, 1.25 mg/kg d-amphetamine; day 8, 0.75 mg/kg d-amphetamine; day 9, water; day 1, 0.5 mg/kg d-amphetamine; day 11, water and day 12, 0.25 mg/kg d-amphetamine. The hypothesis that the degree of response of subjects to one drug was correlated with the degree of the same subjects response to other drugs regardless of dosage was supported. The strength of the relationship between the response tare after saline is inversely related to the dose of the drug used, i.e.,

the higher the dose the lower the correlation at the initial level.

Department of Pharmacology and
Experimental Therapeutics
Boston University School of Medicine
Boston, Mass.

1531 Solle, M., Bauman, R., & Hecht, K. Der Einfluss einer Insulinhypoglykämie auf bedingte Abwehrreflexe der Ratte. [The influence of insulin-induced hypoglycemia on conditioned avoidance reflexes in rats.] Deutsche Gesundheitswesen, 1962, 33, 1381-1388.

In rats treated with 2.0 U/kg Alt-insulin, drowsiness appeared with loss of muscle tone 2-3 hours after injection. Blood glucose levels were measured in relation to injected dosage, as were the various types of inhibition of the avoidance reflex. By means of statistical significance tests, it was found that the induced hypoglycemia was related to increases in the latency period, the duration, and % failures. The differentiation ability remained unchanged. The onset of the inhibitory reactions was not in phase with the onset of hypoglycemia, the latency effect occurring later and lasting longer than the decrease in blood sugar. No statistical relationship between degree of hypoglycemia and strength of inhibition could be established.

Institut für Kortiko-Viszerale Pathologie
und Therapie
Deutsche Akademie der Wissenschaften
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Berlin-Buch, Germany

1532 Liang, H.S., Dodd, R.B., & DeBruine, P.H. A study of the analgesic action of propiomazine and morphine, with a method for assessment of pain in man. Anesthesiology, 1962, 23, 154-155.

In a double-blind study, normal saline, 0.4 mg/cc morphine and 4 mg/cc propiomazine as i.v. infusions were given to normal subjects. Five subjects completed the series of tests: each subject received a different amount of each solution at a different time and an interval of 1 week was allowed between

Behavioral studies
Abstract 1532

tests. Pain was produced either by electric stimulation of s.c. sensory nerves or through ischemic muscular pain produced by pumping up a pneumatic cuff placed on the upper arm. In the 1st case the current intensity shown on the dial of an electronic stimulator was used to assess pain; in the 2nd instance the subject reported as slight, moderate, etc. Morphine produced significant elevations of both pain thresholds and (0.6-2.0 mg) decreased ischemic pain. Subhypnotic doses of propiomazine neither raised the pain threshold nor diminished ischemic pain.

Division of Anesthesiology
Washington University School of Medicine
St. Louis, Mo.

(0.6-2.0 mg) decreased ischemic pain. Subhypnotic doses of propiomazine neither raised the pain threshold nor diminished ischemic pain.

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Washington University School of Medicine
St. Louis, Mo.

See also 1433, 1575.

1533 Boehme, Werner R., Siegmund, Estelle A., Scharpf, William G., & Schipper, Edgar. Structure-activity relationships in a series of anticonvulsant bicyclic acylureas, *Journal of Medicinal and Pharmaceutical Chemistry*, 1962, 5, 769-775.

Anticonvulsant activity against electroshock and pentylenetetrazol-induced convulsions was determined in mice for a series of monocyclic and bicyclic carbonylureas (all administered p.o.) which were synthesized. As well, the procedure of P'an and co-workers (1953) was used to measure hypnotic activity in mice; and dogs were used for 1 compound synthesized. Toxicity and LD₅₀ values were calculated following Litchfield and Wilcoxon (1949). The monocyclic carbonylureas containing a hydrogen atom in the alpha position were of no interest as anticonvulsants. 2-Norbornene-5-endo-carbonylurea, however, afforded good protection against both electroshock and pentylenetetrazol-induced convulsions. Introduction of a methyl group alpha to the carbonylurea chain of the monocyclic and bicyclic derivatives markedly enhanced anticonvulsant activity. Cycloalkenyl and bicycloalkenyl derivatives were more active than their saturated congeners. Anticonvulsant activity was abolished by the introduction of carboxyl, carbomethoxy or carboximide groupings. N³-Acetylation reduced activity slightly but significantly increased the duration of action.

Shulton Inc.
Clifton, N. J.

1534 Rümke, Chr. L., & De Jonge, H. An effect of intraperitoneal saline administration on the duration of hexobarbital narcosis in mice. *Acta Physiol. Pharmacol. Neerlandica*, 1962, 11, 113-122.

The absorption and concentration effects of SKF 525-A (5 mg/kg s.c. or i.p.) on hexobarbital (60 mg/kg i.v. or 75 mg/kg i.p.) sleeping time in inbred mice (TNO strain N) were assessed, using the spontaneous return of the righting reflex as the criterion for the duration of narcosis. Given 2 hours previous to hexobarbital, the i.p. administration of SKF 525-A prolongs

sleeping time. If this pretreatment with SKF 525-A is followed by saline i.p. 1 hour later, the narcosis following i.v. hexobarbital lasts longer than if the saline injection is given s.c. (confirmatory data, Rümke 1962). The narcosis after i.p. hexobarbital lasts longer after an i.p. saline pretreatment than after s.c. saline pretreatment, and the duration of narcosis after i.p. injection of a hexobarbital dose is influenced by the concentration in which it is administered (0.25-0.375 %), i.e., the administration of the weaker solution results in longer narcosis. The local interaction of i.p. administered drugs given a short time after each other, as well as considerations on absorption rates, should be taken into account in studies on the influence of drugs on hexobarbital narcosis and upon other drugs interactions.

Department of Pharmacology
Free University
Amsterdam, The Netherlands

1535 Anderson, Floyd E., Kaminsky, Daniel., Dubnick, Barnard., Klutchko, Sylvester R., Cetenko, Wiaczeslaw A., Gyls, Jonas., & Hart, John A. Chemistry and pharmacology of monoamine oxidase inhibitors: hydrazine derivatives. *Journal of Medicinal and Pharmaceutical Chemistry*, 1962, 5, 221-230.

Seventy aralkyl and acylated hydrazines were synthesized. Their preparation and chemical properties were described. Some pharmacological testing was done and attempts made to correlate activity with structure. The reserpine-challenge test was used to screen these compounds for MAO inhibition in mice; this test detects MAO inhibition only when it occurs in the brain. Selected successful MAO inhibitors were compared according to their ability to elevate brain-serotonin; they exhibited a dose-response relationship. Generally, the same order of potency prevailed in both tests; monosubstituted hydrazines were more active and more toxic than their acyl derivatives, while the carbamates were slightly less active and less toxic and the acetyl derivatives were the least active and the least toxic. Acute toxicity and activity were not always directly related; i.e., p-phenoxy-a-

methylbenzylhydrazine was one of the most active and least toxic of these compounds; also, in vitro and in vivo results were not always comparable. Compounds containing bulky para substituents appear to be the most potent and least toxic.

Warner-Lambert Research Institute
Morris Plains, N. J.

1536 McLennan, H. On the action of 3-hydroxytyramine and dichlorisopropylnoradrenaline on spinal reflexes. *Experientia*, 1962, 18, 278-279.

Chloralose- and urethane- anesthetized cats were studied. The time course of direct inhibition of a monosynaptic reflex arc set up by stimulation of the lateral gastrocnemius nerve was recorded from a ventral root filament. After the administration of 7 mg/kg dichlorisopropyllevarter-enol (dichlorisopropylnoradrenalin) i.v., the inhibition of the reflex was completely unaffected, though this dose was sufficient to largely suppress the inhibition of the reflex brought about by reticular formation stimulation. Therefore, the blocking action of the agent on the latter inhibitory process is not exerted at the level of the mononeuron. Further, the firing pattern of inhibitory Renshaw interneurons of the anterior horn was found to be unaffected by the application to the cord of 5% 3-hydroxytyramine. 3-Hydroxytyramine application may lead to excitation of inhibitory interneurons which make synaptic contact with the motoneurons of the cord.

Department of Physiology
University of British Columbia
Vancouver, British Columbia
Canada

1537 Pustrom, Einar, Prange, Arthue J. Jr., & Cochrane, Carl M. Epinephrine blocking and WY-3041 (5,6, diacetoxy N-methyl indole); a comment on the measurement of blood pressure reactivity. *Journal of Clinical and Experimental Psychopharmacology and Quarterly Review of Psychiatry and Neurology*, 1962, 23, 99-105.

A new drug, 5,6-diacetoxy-N-methyl indole

(WY-3041, 80 mg/day p.o.), was studied in 12 healthy male medical students, aged 23-30 years by the double-blind technique, for its capacity to protect against the systolic hypertensive effects of exogenous epinephrine. Each subject was tested on 3 occasions at 48 hour intervals once with WY-3041, once with a placebo and once with nothing, prior to receiving an i.v. injection of epinephrine (0.0125 mg). The drug exerted no blocking effects on blood pressure reactivity. No significant differences in blood pressure were observed among the 3 types of treatment.

North Carolina Memorial Hospital
University of North Carolina School of
Medicine
Chapel Hill, N. C.

1538 Nielsen, Moller, I., W., Lassen, N., Holm, T., & Petersen, P.V. Central depressant activity of some thiaxanthene derivatives. *Acta Pharmacologica et Toxicologica*, 1962, 19, 87-100.

The neuroleptic activity of 66 thiaxanthene derivatives was investigated and compared with that exhibited by several phenothiazines. Acute i.v. toxicity was determined in mice; LD₅₀ (mg/kg) was measured by the method of Miller and Tainter. Spontaneous motor activity was determined by the dose (mg/kg i.p.) that reduced motility to 50% of control mouse activity, as determined by the method of Kopf et al. Potentiation of hexobarbital anesthesia was determined by administering the test compound (2.5 and 25 mg/kg i.p.) 30 minutes before i.v. injection of 50 mg/kg hexobarbital. The potentiating factor was recorded as the ratio of test animal sleeping time to control sleeping time. Like the phenothiazines, the thiaxanthenes were very potent central depressant drugs with fairly parallel potencies. The following 3 criteria seemed important for maximal central depressant activity: a double bond between carbon 9 and the side chain, substitution at carbon 2 and trans configuration at the double bond.

Department of Pharmacology
Research Laboratories
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Ottolavej 7, Copenhagen Valby
Denmark

1539 Bellville, J. Weldon, Aguto Escarraga, Lourdes, Wallenstein, Stanley L., Wang, Kuo Chen, Howland, William S., & Houde, Raymond W. Antagonism by caffeine of the respiratory effects of codeine and morphine. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 38-42.

The respiratory effects of caffeine (and sodium benzoate), codeine sulfate, and morphine sulfate alone and in xanthine-narcotic combinations were determined by a double-blind factorial study in 10 healthy volunteers. Ten (2 ml) solutions containing normal saline; caffeine 62.5, 125, and 250 mg; morphine sulfate 10 mg; codeine sulfate 60 mg; and narcotic combinations with the 2 lower dosages of caffeine were administered i.m. to 4 subjects, while the remaining 6 received an identical dosage schedule except for the administration of caffeine alone. According to the alveolar ventilation-alveolar P_{CO_2} response curve, caffeine alone did not cause a significant stimulation of respiration, perhaps due to low doses or insensitive techniques. Morphine (10 mg) produced a significantly greater degree of respiratory depression than codeine (60 mg). The simultaneous administration of caffeine with codeine or morphine produced a statistically significant decrease in respiratory depression caused by the narcotics. The dose-effect relationship is the greater the amount of caffeine, the greater the decrease in respiratory depression. The results, which suggest that the greater the respiratory depressant effects of the narcotic, the more effective caffeine may be in its antagonism, are in agreement with the findings of Stroud et al. (1955), who observed that aminophylline prevented meperidine-induced respiratory depression.

Department of Anesthesiology
Memorial Hospital
New York, N. Y.

1540 Mattila, M. The effects of morphine and nalorphine on the small intestine of normal and morphine-tolerant rat and guinea-pig. *Acta pharmacologica et toxicologica*, 1962, 19, 47-52.

Morphine and nalorphine receptor mechan-

isms were studied in rat intestine. Tests were conducted in vitro on pieces of small intestine from fasting male rats, stimulated at 6-minute intervals. Among drugs tested for degree of inhibition were nicotine (15-150 μ g), pilocarpine (3-15 μ g), barium chloride (250-750 μ g) and 5HT (0.2-0.5 μ g). Morphine (10-500 μ g) and nalorphine (100-300 μ g) were added 30 seconds before stimulation. Intestine from morphine-tolerant rats, and normal and morphine-tolerant guinea pigs, was also studied. Morphine proved to be an effective inhibitor of nicotine induced contractions and a poor inhibitor of those caused by 5HT and pilocarpine in rat intestine; all these contractions were prevented more readily by nalorphine. No morphine-nalorphine antagonism occurred in rat intestine. Intestine from some addicted rats was extremely sensitive to nalorphine; this was not observed in the intestine of tolerant guinea pigs, which showed a marked morphine tolerance.

Department of Pharmacology
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1541 Chilton, J., & Stenlake, J.B. Dissociation constants of some compounds related to lysergic acid. *Journal of Pharmacy and Pharmacology*, 1962, 14, 367-370.

Dissociation constants were determined for ergometrine, ergometrinine, LSD, isolysergic acid and a number of alkanolamides of 3-dimethylaminopropionic acid, 1-methylhexahydronicotinic acid and arecaidine. The similarity of pK (amide) values for the alkanolamides to that for ergometrine offered evidence that such values might be taken as an indication of amino-carboxyl distances. The dissociation constants were determined by the method of Chilton and Stenlake in an aqueous medium containing carbonate-free potassium hydroxide; LSD and isolysergic acid required a small amount of carbonate to facilitate solubility (they were back-titrated immediately with dilute acid).

Department of Pharmacy
The Royal College of Science and Technology
Glasgow, Great Britain

1542 Supek, Z., Uroić, B., Gjuriš, V., & Marijan, N. The effect of adrenergic blocking agents and of chlorpromazine on blood pressure increase by vasopressin and angiotensin. *Journal of Pharmacy and Pharmacology*, 1962, 14, 284-287.

The i. v. influence of chlorpromazine (2-5 mg/kg), hydergine (0.3-0.9 mg/kg), dibenamine (25 mg/kg) and tolazoline (20-40 mg/kg) on the mean arterial response to i. v. vasopressin (0.1 I.U./kg), angiotensin (0.07 mg/kg) and barium chloride (0.5-1.0 mg/kg) was investigated in anesthetized mongrel dogs. The adrenergic blocking agents potentiated the pressor response to vasopressin but did not affect responses to angiotensin or barium chloride. Chlorpromazine potentiated the response to both vasopressin and angiotensin; this potentiation was not due to a decrease in blood pressure produced by adrenergic blocking or by chlorpromazine.

Department of Pharmacology
University of Zagreb
Zagreb, Yugoslavia

1543 Sloan, Jewell W., Brooks, J.W., Eisenman, Anna J., & Martin, W.R. Comparison of the effects of single doses of morphine and thebaine on body temperature, activity, and brain and heart levels of catecholamines and serotonin. *Psychopharmacologia*, 1962, 3, 291-301.

Single doses of morphine (15-60 mg/kg i. p.) were given to equal numbers of randomized Wistar rats, which were sacrificed 4 hours after treatment. Brains and hearts were analyzed for catecholamines; brains were also analyzed for serotonin. Animals were observed for changes in activity and body temperature. There were no significant changes in heart catecholamines, brain serotonin or catecholamines 4 hours after morphine. Brain catecholamines increased 2 hours after injection of morphine (60 mg/kg). Doses of 15-30 mg/kg resulted in an initial depression of activity followed by increased activity and body temperature, 60 mg/kg produced profound depression of activity and body temperature, which was maximal at 2 hours. Respiratory depression also occurred in these animals, with cyanosis in half of the cases. None

showed cyanosis with 15 mg/kg and very few with 30 mg/kg. In a comparative study, 20 mg/kg of thebaine produced a moderate decrease in brain and heart catecholamines, but no significant changes in brain serotonin within 30-60 minutes after drug administration. Fifteen of the 26 animals had convulsions, 7 had major seizures and 4 died. Animals appeared sedated inbetween seizures. No hyperthermia was observed.

Addiction Research Center
NIMH, USPHS
Lexington, Ky.

1544 Azima, H., Arthurs, Dorothy, & Silver, A. The effects of chlordiazepoxide (Librium) in anxiety states. A multi-blind study. *Canadian Psychiatric Association Journal*, 1962, 7, 44-50.

The antianxiety properties of chlordiazepoxide (Librium) were evaluated in a multi-blind study on 2 randomly selected groups of 92 patients each (75 neurotics and 17 psychotics), 1 group receiving p.o. an average daily dose of 70 mg for an average of 3 weeks, the other (controls) receiving placebo; and a 3rd group of 15 neurotics receiving placebo and drug sequentially. Chi² analysis of data revealed that chlordiazepoxide had a highly significant effect ($P < 0.001$) in neurotic states, but not in psychotics, while analysis of subgroup data in neurotics showed a statistically significant improvement rate in anxiety states and mixed states ($0.01 > P > 0.001$), but not in obsessive and depressive states. The most common side effects were headache, dizziness, hand tremors, drowsiness, nausea and vomiting. The efficacy of chlordiazepoxide as an adequate antianxiety and antitension drug may be limited to anxiety reactions and mixed neurotic states.

Allan Memorial Institute
McGill University
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Canada

1545 Horovitz, Zola P., & Chow May-I. Effects of centrally acting drugs on the correlation of electrocortical activity and

wakefulness of cats. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 127-132.

Cats with chronically implanted electrodes were used in the study of atropine, tetrahydroaminacrin (THA), N-ethylpiperidyl, ethotrimeprazine, physostigmine salicylate, chlorpromazine, triflupromazine and imipramine, all injected i. p. Responses i. e., behavior, and electrocortical recordings were used as test parameters. Atropine and ethotrimeprazine produced dissociation with the latter being about 10 times as potent. Physostigmine and THA caused the opposite type of dissociation with normal or low levels of behavior being associated with a fast low voltage electrocorticogram. Imipramine did not produce any dissociation or stimulation but did depress the animal's behavior, as did chlorpromazine and triflupromazine.

Squibb Institute for Medical Research
New Brunswick, N. J.

1546 Gabourel, John D., & Comstock, John P. Effect of diacetylmonoxime on the action of convulsant and sedative-hypnotic barbiturates. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 122-126.

Male Swiss-Webster mice and male Wistar rats were employed in the assessment of diacetylmonoxime (DAM). Also rabbit microsomes were used for in vitro metabolic studies according to Gillette et al. (1957). Hexobarbital was assayed photometrically and C¹⁴-labeled pentobarbital by its radioactivity. Mice and rats pretreated with DAM lose their righting reflex when given injections of 25-35 mg/kg 3,5-dimethylbutylethyl barbiturate (DMBEB). Although these doses of DMBEB cause motor convulsions and death in saline-injected controls, DAM-treated animals do not exhibit motor convulsions nor do they die. DAM-pretreatment was also shown to prolong barbiturate-induced loss of righting reflex in mice, rats and rabbits, but it failed to inhibit the metabolism of either hexobarbital or DMBEB by liver microsomes. When mice or rats were injected with DAM on

awaking from barbiturate sleep, they again lost their righting reflex and studies in mice with C¹⁴-labeled pentobarbital showed that here DAM did not elevate the brain barbiturate level and therefore prolongation of the righting reflex is brought about either by a direct central action of DAM or by barbiturate potentiation of the weak neuromuscular blocking action of this oxime.

Department of Pharmacology
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Palo Alto, Calif.

1547 Maynert, E. W., & Kaji, Hideko, K. On the relationship of brain γ -aminobutyric acid to convulsions. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 114-121.

Clonic seizures were electrically-induced in Swiss mice and Sprague-Dawley rats. Brain GABA was estimated chromatographically after sacrifice. Mice injected i. p. with thiosemicarbazide showed a significantly smaller decrease in brain GABA than that found in animals similarly treated with semicarbazide, acetone semicarbazone, thiocarbohydrazide, isonicotinic acid hydrazide or 3-deoxypyridoxine phosphate (all at 2.67 μ M/g i. p.). Compared with the hydrazides, methylhydrazine and 1-phenyl-2-hydrazinopropane caused little change in GABA while a convulsive dose of hydrazine caused an increase in brain GABA. Large doses of succinonitrile (500 μ g/g) and diphenylhydantoin (200 μ g/g) were almost as effective as hydrazides in lowering GABA. Metrazol, picrotoxin and insulin caused smaller decreases and reserpine had no effect. Brain GABA in mice and rats was only elevated in level by hydrazine and hydroxylamine, hydrazine being more effective and less toxic. Neither or these compounds altered the incidence or duration of the electrically-induced clonic seizures or modified the pattern of a maximal seizure. Mice could not be protected against pentylenetetrazol seizures by hydrazine and hydrazine-treated mice injected with semicarbazide exhibited maximal seizures at supernormal concentrations of brain GABA. Hydrazide-induced convulsions may possibly cause a supernormal utilization

of GABA for energy-yielding reactions in the brain.

Johns Hopkins University School of
Medicine
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1548 Davis, W.M. Day-night periodicity in pentobarbital response of mice and the influence of socio-psychological conditions. *Experientia*, 1962, 18, 235-237.

Mice were given the customary 60 mg/kg dose of pentobarbital i. p. and the illumination in their environment automatically controlled. Twelve hours of darkness alternating with 12 hours of light were provided which corresponded approximately to the natural daily cycle. The anesthetic effect was marked during the day and weak at night; this was true for both experiments run at 26°C and at 36°C. The periodicity of analgesic effect disappeared when the mice were kept under continuous illumination and the degree of periodicity diminished when mice were kept isolated instead of grouped.

University of Oklahoma College of
Pharmacy
Norman, Okla.

1549 Kraupp, O., Bernheimer, H., Heistracher, P., Papistas, D., & Schiefthaler, Th. Die Wirkung von Iproniazid sowie i. p. Zufuhr von Katecholaminen und ihrer O-Methyl-derivate auf die renale Ausscheidung von Metanephrin und Normetanephrin an der Ratte. [Effect of iproniazid and i. p. administration of catecholamines and their o-methyl derivatives on the renal excretion of metanephrine and normetanephrine in rats.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 459-467.

Treatment of rats with iproniazid (50 mg/kg/day i. p. for 3 days) increased the urinary excretion of normetanephrine from negligible values to 46 µg/kg/24 hours; the recovery of metanephrine from the urine after i. p. administration of 400 µg/kg epinephrine or 800 µg/kg metanephrine

varied from 11-29% and the recovery of normetanephrine from the urine after i. p. administration of 400 µg/kg levarterenol or 800 µg/kg normetanephrine from 7 and 13%, respectively, to 11 and 19%. The urinary output of normetanephrine was also increased after metanephrine or dopamine administration in iproniazid-treated rats, but not after adrenalone or noradrenalone. There was no detectable urinary excretion of metanephrine without previous administration of catecholamines. The excretion of levarterenol as such was also increased by iproniazid.

Pharmakologisches Institut
Universität Wien
Vienna, Austria

1550 Court, William E. African *Rauwolfia* species. Part II. The structure of the root and stem of *Rauwolfia mombasiana* Stapf. *Journal of Pharmacy and Pharmacology*, 1962, 14, 22-36.

Rauwolfia mombasiana, an East African shrub with a high reserpine yield, was recommended as a substitute or adulterant for the roots of *Rauwolfia vomitoria*. The morphology of the root and stem is described and illustrated; a comparison to other African species is presented. The radial, tangential and longitudinal sections are described histologically.

Department of Pharmacy
City of Liverpool College of Technology
Liverpool, Great Britain

1551 Winne, D. Die Wirkung einiger Schlaf- und Narkosemittel bei röntgenbestrahlten Mäusen. [The effect of some hypnotics and narcotics on X-irradiated mice.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 212-231.

Male mice were subjected to total body irradiation 4-5 days before administration of various drugs and the duration of the hypnotic effect was measured. Irradiation prolonged the effects of cyclobarbitol, hexobarbital, hydroxydione, pentobarbital, thiopental, tribromoethanol, chloralhydrate and methypylon, but shortened

that of urethane. Control experiments showed that the effect of X-ray was not due to decreased food consumption, and administration of glucose had no effect. The prolongation of the hypnotic effect is probably due to interference with drug catabolism.

Medizinische Forschungsanstalt
Max Planck Gesellschaft
Göttingen, Germany

1552 Holck, Harald G.O., Demaree, Gale E., & Kaji, Hideko Katayama. Effects of β -diethylaminoethyl diphenylpropylacetate hydrochloride on three convulsants and on propallylonal. *Journal of Pharmaceutical Sciences*, 1962, 51, 739-742.

The effects of β -diethylaminoethyl diphenylpropylacetate (SKF 525-A) on 3 convulsants and propallylonal was studied in Swiss mice and Holtzman rats at various doses. The LD₅₀'s of nikethamide, pentylenetetrazol and picrotoxin were increased by pretreatment of mice 1 hour before drug injection with SKF 525-A. SKF 525-A markedly prolonged the hypnotic effect of propallylonal without increasing the number of delayed deaths in rats. The maximal picrotoxin action in mice pretreated with SKF 525-A s.c. developed in about 4 hours, was still marked at 8 hours, and was lost by 16 hours. SKF 525-A induced maximal effects when given i.p. immediately prior to picrotoxin; it also markedly facilitated the potency of picrotoxin in normal rats and in those receiving barbitol, by a multiple injection technique. Using this same technique, barbitol greatly increased LD₅₀'s of pentylenetetrazol and picrotoxin in rats. SKF 525-A did not influence the toxicity of pentylenetetrazol in normal rats or in those receiving barbitol by the multiple injection method.

Department of Pharmacology
College of Pharmacy
University of Nebraska
Lincoln, Neb.

1553 Kapila, Kanti, & Arora, R.B. Anticonvulsant activity of procaine and its five congeners against experimentally

induced convulsions. *Journal of Pharmacy and Pharmacology*, 1962, 14, 253-254.

Procainamide, procaine and its 4 congeners were studied for anticonvulsant activity and compared with phenytoin against maximal electroshock and leptazol-induced seizures in rats. Neurotoxicity and acute toxicity were determined; ED₅₀, TD₅₀, LD₅₀, therapeutic indices and protective indices of the drugs were calculated. These compounds were effective only against maximal electroshock seizures, they were effective within 10 minutes and remained so for 2-3 hours, while the effect of phenytoin lasted much longer. Clonic convulsions preceded death during acute toxicity studies. Procaine, and to a greater degree, its methyl substituted congeners, had higher protective and therapeutic indices than did phenytoin, while these indices were lowest for procainamide.

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1554 Werdinius, Bengt. Effect of temperature on the action of reserpine. *Acta Pharmacologica et Toxicologica*, 1962, 19, 43-46.

An attempt was made to reproduce the results reported by previous authors on the effects of temperature on reserpine action. Male rats were exposed to various temperatures (-10°, 4° and 37°C) for various periods up to 16 hours, then given reserpine (1.0-2.5 mg/kg i.p.). After 4 additional hours in the same environment the animals were sacrificed and their brains analyzed for 5HT content (by a slight modification of Bertler's method). Controls were run in parallel, because of considerable normal variation in brain 5HT. All animals treated with reserpine were sedated, with ptosis and characteristic hunched posture, irrespective of thermal environment, 5HT content was comparably lowered by reserpine under all temperature conditions.

Department of Pharmacology
University of Göteborg
Göteborg, Sweden

- 1555 Feldman, Shaul, & Wagman, Irving H. Hypothalamic effects on spinal reflexes and their alteration by pentobarbital. *Experimental Neurology*, 1962, 5, 250-268.

Alterations in hypothalamic effects on spinal reflexes were studied at various levels of pentobarbital anesthesia in 15 intact cats. Potentials evoked in the hypothalamus upon peripheral stimulation were studied concurrently. In immobilized and lightly anesthetized animals, high-frequency hypothalamic stimulation usually potentiated monosynaptic and depressed polysynaptic reflexes. Moderate pentobarbital anesthesia produced a diminution of hypothalamic effects of spinal cord reflexes with disappearance of the peripherally evoked hypothalamic potentials. Deepening of anesthesia abolished hypothalamic facilitation of the spinal monosynaptic reflex. Hypothalamic stimulation had little or no effect on persistent polysynaptic response. High-voltage, secondary, long-latency potentials were evoked in the hypothalamus by peripheral nerve stimulation at this stage of deep anesthesia. The effects noted were due primarily to the actions of pentobarbital in the hypothalamus and only partly to the effect of anesthesia on the spinal mechanisms. In the lightly anesthetized or immobilized intact animal the facilitatory brainstem regions have a predominant effect on spinal cord reflexes, and anesthesia (or decerebration) attenuates this facilitatory effect, thus allowing the inhibitory effect of the bulbar reticular formation on the spinal cord to be shown.

Department of Neurology
Mount Sinai Hospital
New York, N. Y.

- 1556 Essig, Carl F. Convulsive and sham rage behaviors in decorticate dogs during barbiturate withdrawal. *Archives of Neurology*, 1962, 7, 471-475.

Three decorticate dogs, 27 to 37 days after surgery, and intact controls received increasing amounts of p.o. barbitol until final daily dose levels of 118 to 178 mg/kg were attained (in periods varying from 202 to 372 days). Following abrupt withdrawal,

all of the control dogs, but none of the decorticate dogs, developed tonic-clonic convulsions. One decorticate dog exhibited 2 episodes of sham rage behavior that included violent motor activity, barking, trembling, and excess salivation. Two of the decorticate dogs were intoxicated and withdrawn a 2nd time. Final daily dose levels attained were 190 and 248 mg/kg and both developed sham rage as well as convulsive behavior during the 2nd withdrawal. The seizure patterns were modified from normal, and it was concluded that the decorticate dog requires much higher final intoxication levels of barbiturate than the intact animal in order to develop abstinence convulsions that are not as intense. In the intact brain the cerebral cortex probably plays a facilitatory role in barbiturate convulsions, but it does not seem to be a necessary site of their origin or an obligatory substrate thereof.

Addiction Research Center
NIMH, USPHS
Lexington, Ky.

- 1557 Bagdon, Walter J., & Mann, David E., Jr. Chlorpromazine hyperthermia in young albino mice. *Journal of Pharmaceutical Sciences*, 1962, 51, 753-755.

Chlorpromazine (1 mg/kg i.p.) effects on body temperature were studied in 1321 mice (HTF/strain) 10-38 days of age, divided into 9 groups of 116-238 per group. The maximum intragroup age variation was 15 hours. Half of each group served as controls. Sex distribution was fairly even within all groups except the youngest. Temperatures were determined orally with a probe immediately before and 30 minutes after each injection. Chlorpromazine caused significant hyperthermia in 10-15 day old mice and hypothermia in 35-38 day old mice. While an age-conditioned effect was demonstrated, no sex-influenced effect was found.

School of Pharmacy
Temple University
Philadelphia 40, Pa.

- 1558 Garattini, S., Giachetti, A., Jori,

A., Pieri, L., & Valzelli, L. Effect of imipramine, amitriptyline and their monomethyl derivatives on reserpine activity. *Journal of Pharmacy and Pharmacology*, 1962, 14, 509-514.

The effects of imipramine, amitriptyline and their N-monomethyl derivatives (all 7.5-30 mg/kg i.p.), on reserpine (2.5-5.0 mg/kg i.v. or i.p.) activity was studied in female Sprague-Dawley rats, Swiss mice and the zebra fish (*Brachydanius rerius*). Demethylimipramine and demethylamitriptyline reduced the reserpine-induced hypothermia in rats more readily than did the parent compounds, imipramine and demethylimipramine decreased the severity of gastric ulcers induced by reserpine in restrained rats more so than did amitriptyline or its desmethyl derivative; desmethylimipramine did not prevent the decrease in brain amine level induced by reserpine. Imipramine, but not demethylimipramine, antagonized leptazol (0.5%) convulsions, failed to potentiate the central effects of 5HTP and 5HT, and did not prevent the hypothermia induced by 5HT, α -methyl dopa (500 mg/kg i.p.) or chlorpromazine (10 mg/kg i.p.).

Department of Pharmacology
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1559 Hartry, Arlene L. The effects of reserpine on the psychogenic production of gastric ulcers in rats. *Journal of Comparative and Physiological Psychology*, 1962, 55, 719-721.

The effects of low dosages of reserpine (0.1 mg/kg i.m.) on the psychogenesis of gastric ulcers was studied in 28 male Wistar rats, with restraint stress used to induce ulceration (Bonfils et al. 1957). Four experimental conditions were investigated: immobilization (plus hunger and thirst) accompanied by injection of reserpine, immobilization (plus hunger and thirst) alone, reserpine alone and hunger and thirst alone. Ulcers occurred primarily in the immobilization-reserpine group and secondly in the immobilization-no reserpine group. Titration revealed less stomach

acidity in ulcerated rats. No relationship was observed between weight loss and frequency of ulceration. Titration values indicated that ulceration was accompanied by increased gastric motility or decreased gastric secretion. Restraint stress may provoke the physiological reactions of anger rather than anxiety.

[No address]

1560 Malone, Marvin H., & Roth, Robert H., Jr. Yohimbine potentiation of reserpine blepharoptosis. *Journal of Pharmaceutical Sciences*, 1962, 51, 345-348.

The mouse ptosis assay developed by Rubin et al. was randomly employed in 216 mice to determine the effects of yohimbine (2-16 mg) on potentiation of reserpine (2-8 mg/kg). The oral LD₅₀ was 36.5 mg/kg for yohimbine and 150 mg/kg for reserpine. Various reserpine-yohimbine mixtures were assayed against reserpine alone in 4 balanced log dose-response assays. Maximal mean ptotic effects following reserpine administration occurred within 10 hours. Yohimbine produced detectable ptosis at doses of 16 mg/kg but not at 8 mg/kg. Statistical treatment involved analysis of variance, factorial analysis, and calculation of potency and confidence limits according to the method of Bliss. Peak potentiation occurred at 3 hours for 1:1 and 1:2 reserpine-yohimbine mixtures, while peak effects were achieved at 10 hours with the 1:4 mixture, indicating considerable distortion by yohimbine of any ptotic assay documenting only reserpine activity. Yohimbine, in a 1:1 ratio with reserpine, potentiated ptosis for about 5 hours, ceased to be effective within 10 hours and may have aided reversal of residual ptosis by 24 hours. With a 1:2 ratio, ptosis was unaffected at 24 hours. Complete potentiation was obtained with yohimbine in a 1:4 ratio at all times. Males were considerably more susceptible to reserpine-induced ptosis than females. Yohimbine lacked true ptotic activity but potentiated reserpine-induced blepharoptosis without altering slope or dose-response relationships, thus indicating that the mechanism of reserpine action may

be dependent upon depletion of levarterenol rather than upon release of serotonin.

Division of Pharmacology
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1561 Schumann, E.L., Paquette, L.A., Heinzelman, R.V., Wallach, D.P., Vanzo, J.P., & Greig, M.E. The synthesis and γ -aminobutyric acid transaminase inhibition of aminooxy acids and related compounds. *Journal of Medicinal and Pharmaceutical Chemistry*, 1962, 5, 464-477.

A series of 36 GABA analogues failed to inhibit GABA- α -keto glutaric acid (AKG) transaminase in vitro and in vivo. These compounds were also unable to raise GABA brain levels. Several of the 46 aminooxy derivatives synthesized were fairly active inhibitors of GABA-AKG transaminase in vitro and in vivo. All compounds were tested for their protective activity against thiosemicarbazide-induced convulsions (8 rats or mice received 10, 25 or 50% of the LD₅₀ 1 hour before receiving thiosemicarbazide, 20mg/kg i.p.), and the resultant degree of protection paralleled the in vivo GABA transaminase inhibition. A significant degree of in vivo activity was limited to several α -amino-oxyacids or their easily hydrolyzed derivatives. No compound showed activity superior to that of aminooxyacetic acid. Most compounds were prepared by alkylation of a hydroxylamine derivative in the presence of base, followed by hydrolysis of the protecting group. Relevant data on all compounds is presented in tabular form.

Upjohn Company Research Laboratories
Kalamazoo, Mich.

1562 Remmer, H., Siegert, M., Nitze, H.R., & Kirsten, I. Die Gewöhnung an langwirkende Barbiturate. [Tolerance to long-acting barbiturates.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 468-478.

Administration of phenobarbital (110 mg/kg) or barbital (150 mg/kg) s.c. to rats 3 times

a week for 4 weeks produced no decrease in the duration of anesthesia following a test i.p. dose, compared to controls, although 5 out of 28 male rats and 17 out of 27 females died. Thus there seems to be chronic poisoning in females, with sufficient accumulation to produce tolerance. Daily administration of phenobarbital (50 mg/kg b.i.d., s.c.) or barbital (200 mg/kg/day s.c.) did produce tolerance in rats, as measured by an increase in the concentration measured in the blood when the animals awoke. In dogs, which eliminate phenobarbital more slowly, daily p.o. administration of increasing doses (2-30 mg/kg) also produced tolerance, as measured by the disappearance of ataxia at increasingly high blood levels. This tolerance was no longer demonstrable after 11 days without treatment when practically all of the phenobarbital had been eliminated. This type of tolerance is to be distinguished from the tolerance to short-acting oxidizable barbiturates due to an increase in their catabolic rate.

Pharmakologisches Institut
Freie Universität
Berlin, Germany

1563 Sammalisto, Lasse. Effect of glutamine on intoxication caused by ethyl alcohol. *Nature*, 1962, 185, 185.

A total of 57 fasting rats were divided into 7 groups of 6-10 animals which were tested for ethyl alcohol intoxication by placing each rat on an inclined plane with a rough surface; at a given angle of inclination the rat slid down the plane. Intoxicated rats slid down at lower angles than normal ones. The performance while intoxicated was expressed as a percentage of the value obtained while sober. Animals received the alcohol (3.0-4.5 mg/kg intragastrically) as a 30% v/v solution, glutamine [dose not stated] was administered in the alcoholic solution. Glutamine did not effect the blood alcohol level. However, it did offer variable degrees of protection against intoxication, which were contingent upon genetic and environmental conditions. Glutamine effects depended upon the role played by this compound in brain metabolism during

alcohol intoxication.

Research Laboratories of the State
Alcohol Monopoly (Alko)
Helsinki, Finland

1564 Callingham, B.A., & Cass, Rosemary.
The effects of bretylium and cocaine on
noradrenaline depletion. *Journal of*
Pharmacy and Pharmacology, 1962, 14,
385-389.

Rats were used to study the effects of
bretylium (30 mg/kg s.c.) and cocaine
(10-50 mg/kg s.c.) on levarterenol
depletion. Reserpine was administered
s.c. at 0.1-1.0 mg/kg and guanethidine at
10 mg/kg to see if bretylium or cocaine
might reduce their ability to deplete rat
heart and spleen levarterenol levels; this
reduction did not occur. Rats were
sacrificed 6-18 hours after drug injection
and catecholamine content (epinephrine and
levarterenol) of heart and spleen assayed
(method of Cass and Spriggs 1961) and
expressed in terms of levarterenol. In
additional experiments, 50 mg/kg cocaine
failed to reduce the pressor action of
physostigmine (20 µg i.v.) in anesthetized
rats; in fact it slightly potentiated the
response. Bretylium probably acts by
preventing levarterenol release, while
cocaine prevents releasing agents from
reaching levarterenol depots.

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1565 Schmidt, G., & Meisse, P. Zentrale
Wirkungen von Cocainhomologen und ihre
Beeinflussbarkeit durch Reserpin oder
Adrenolytica. [Central effects of cocaine
homologs and the effect of reserpine or
adrenolytic agents.] *Archiv für Experi-*
mentelle Pathologie und Pharmakologie,
1962, 243, 148-161.

Pretreatment of guinea pigs with reserpine
(5 mg/kg s.c.) abolished or markedly
decreased the specific central sympathetic
response to l-n-cocaine (increased motility,

increased body temperature and hyper-
glycemia) and depressed the convulsive
action, but had no effect on the toxic
effects of d-4-cocaine. Similarly the
ptosis due to reserpine was temporarily
abolished by l-n-cocaine but not by d-4-
cocaine. Pretreatment with iproniazid
(100 mg/kg) potentiated the effects of
l-n-cocaine but had no effect on the
response to d-4-cocaine. The adrenolytic
agents yohimbine (5 mg/kg s.c.) and
phentolamine (0.05 mg/kg intracisternally)
counteracted the pyrogenic effect of l-n-
cocaine, but s.c. phentolamine was
ineffective. In mice analgesic properties
were shown by l-n-cocaine but not by
d-4-cocaine. The psychopharmacological
effects of l-n-cocaine are assumed to be
mediated by an increased sensitivity to
catecholamines in the CNS.

Pharmakologisches Institut
Universität Göttingen
Göttingen, Germany

1566 Friebe, H., & Kuhn, H.F. Über
husten- und atemdepressorische Wirkung.
[Depressant effects on coughing and
respiration.] *Archiv für Experimentelle*
Pathologie und Pharmakologie, 1962, 243,
162-173.

In an attempt to differentiate pharmacologic-
ally between the regulatory systems for
coughing and respiration, experiments were
carried out on male guinea pigs forced to
cough by inhalation of SO₂. Drugs were
administered s.c. 30 minutes before SO₂.
In other experiments, respiratory rate and
minute volume were recorded kymograph-
ically. The ED₅₀ for cough suppression
was smallest with l-phenethyl-4-(propin-
2-yl)-4-propionoxypiperidine (1.6 mg/kg)
and highest for hexobarbital (77.0 mg/kg).
Codeine, pipazethate and 2-aminoindane all
had ED₅₀ values of 14.5-15.5, while
pentoxyverin was 50.0 mg/kg. Respiration
was markedly depressed by hexobarbital,
even at 50 mg/kg, and moderately by
codeine, but stimulated by 2-aminoindane;
the other 3 drugs had little effect on
respiration. Isoprenaline (0.01 mg/kg s.c.)
did not alleviate the depression produced by
hexobarbital, but had some effect on that
produced by codeine. When given after

hexobarbital (50 mg/kg), 4 of the other antitussives seemed to potentiate the depressant effect on respiration, while 2-aminoindane again stimulated respiration. The results suggest that the central mechanism of the cough reflex is to a considerable extent independent of the central mechanism of the respiration.

Pharmakologisches Institut
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Bonn 53, Germany

1567 Klärner, Paul. Über den Einfluss von Barbituraten, Thiobarbituraten und Barbitursäure auf cellulläre Potentiale und Kontraktionen des Meerschweinchenvorhofes. [The effect of barbiturates, thiobarbiturates and barbituric acid on cellular potentials and contractions of the guinea pig auricle.] Archiv für Experimentelle Pathologie und Pharmakologie, 1962, 243, 269-278.

Comparative studies of hexobarbital, pentobarbital, thiopental, methitural and barbituric acid in the electrically stimulated guinea pig auricle showed that low concentrations of all these drugs first prolonged the 90% repolarization time, while high concentrations produced increasing shortening of the 20%, 50% and 90% repolarization time. Very high concentrations decreased the resting potential. Only thiobarbiturates affected the rhythm of auricular contraction, and they were more effective than barbiturates in increasing the latent period. Thus, at clinical dosage, barbiturates are less cardiotoxic than thiobarbiturates. Barbituric acid itself prolonged all phases of repolarization only at high concentrations. These drugs apparently act by changing ionic permeability.

Pharmakologisches Institut
Universität Mainz
Mainz, Germany

1568 Klinger, W., & Kersten, L. Die analeptische Wirkung von Vanillinsäure-diethylamid. [The analeptic effect of vanillic acid diethylamide.] Acta Biologica et Medica Germanica, 1962, 9, 67-78.

Comparative studies of vanillic acid diethylamide, metrazol and nikethamide in

mice, rats, guinea pigs, rabbits and cats showed that vanillic acid diethylamide has a marked analeptic effect on respiration, often surpassing that of metrazol, but a less marked effect on blood pressure. The LD₅₀ was 43 mg/kg i. p. in mice and 17 mg/kg in rats. Daily injections of 20% of the LD₅₀ were well tolerated. Vanillic acid diethylamide had no peripheral vascular effect but did show adrenergic effects on the isolated guinea pig auricle and spasmolytic effects on the isolated intestine. There was no effect on coronary vessels, and no antagonism to barbiturate, chloral hydrate or paraldehyde.

Institut für Pharmakologie
Friedrich Schiller Universität
Jena, Germany

1569 Bergmann, Felix, Gutman, Jehuda, & Chaimovitz, Moshe. Comparison of the influence of graded doses of phenothiazines and pentobarbitone on central nystagmus. Experimental Neurology, 1962, 5, 210-217.

The effects of perphenazine (0.015-3.5 mg/kg), chlorpromazine (0.025-2.0 mg/kg) and thioridazine (0.010-2.0 mg/kg) on central nystagmus in 35 conscious rabbits were determined, stimuli were applied through bipolar, concentric implanted electrodes and results were monitored. All 3 drugs gave essentially the same results; small amounts (10-25 µg/kg) depressed the response, while doses above 100 µg/kg produced a biphasic reaction, i. e., enhancement (increased frequency of eye movements) for 1 or 2 hours followed by prolonged depression. A similar gradation was also observed with pentobarbital, except that its effects were restricted to shorter periods of time. Different mechanisms are involved in the action of the phenothiazines and pentobarbital based upon their antinystagmus activity. Interpretation of the results is based on the heterogeneity of the nervous elements in the circuit which produce nystagmus.

Department of Pharmacology
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Jerusalem, Israel

570 Carson, Richard P., & Domino, Edward F. Synergistic and antagonistic effects of premedication on general anesthetics in mice. *Anesthesiology*, 1962, 23, 187-192.

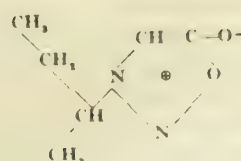
The effects of preanesthetic medication on the anesthetic and lethal concentrations of general anesthetics were studied in untreated, saline-control and drug-treated mice. Premedication (all drugs given i. p.) with subanesthetic doses of pentobarbital (20-30 mg/kg) and phenobarbital (65 mg/kg) had a synergistic effect on the anesthetic concentration of diethyl ether, halothane, and chloroform but no significant effect on their lethal concentration. Atropine or scopolamine premedication (1 mg/kg) had no synergistic or antagonistic effect on the anesthetic or lethal actions of diethyl ether, halothane or chloroform. Morphine premedication (5 mg/kg) did not affect time to anesthesia with diethyl ether and halothane but prolonged time to death. Chlorpromazine and promethazine produced variable results with doses of 5 mg/kg but at 15 mg/kg, chlorpromazine reduced time to anesthesia and prolonged the time for death for diethyl ether and halothane but not chloroform. In equal doses, promethazine was less effective. Pentobarbital and phenobarbital appear to have a selective effect of increasing the anesthetic but not the lethal potency of diethyl ether, chloroform and halothane. Pentobarbital premedication should therefore improve the therapeutic index of these agents. The variable results found with the phenothiazine derivatives, particularly with smaller doses, rules out definitive conclusions on their utility.

Department of Pharmacology
University of Michigan
Ann Arbor, Mich.

1571 Kier, Lemont B., Fox, Lauretta E., Dhawan, D., & Waters, I. W. A new class of central nervous system stimulants. *Nature*, 1962, 195, 817-818.

An N-alkyl sydnone called compound I:

[N-isobutylsydnone]:



was studied pharmacologically. In male brown mice (C57B x 1101 hybrids), the s.c. LD₅₀ is ca. 135 mg/kg and the convulsive dose ca. 117 mg/kg. Pentetrazole under the same conditions had an LD₅₀ of ca. 75 mg/kg. Convulsions began less than 1 minute after administration, and caused ticking in the facial musculature and forelimbs. This was followed by clonic movements which frequently developed an extensor component and almost all animals died in tonic convulsions. A spinal cat, transected at C-1, did not convulse at 100 mg/kg; 2 decerebrate cats showed definite convulsive patterns at 200 mg/kg. When 41 mg/kg of either compound I or pentetrazole was administered i. v. to a dog (given sufficient pentobarbital i. v. to cause apnea) the more favorable response and rise in blood pressure was obtained with compound I. Respiratory stimulation appeared to be predominantly central as there was little decrease of activity after vagotomy or carotid sinus denervation. Compound I did not potentiate acetylcholine and produced no acetylcholine esterase inhibition. There was no antispasmodic activity against acetylcholine or histamine in guinea pig ileum. No spasmodic activity was noted in isolated tissue although a positive Straub test was observed in Compound I-treated mice.

College of Pharmacy
University of Florida
Gainesville, Fla.

1572 Drain, D. J., Horlington, M., Lazare, R., & Poulter, G. A. The effect of α-methyl DOPA and some other decarboxylase inhibitors on brain 5-hydroxytryptamine. *Life Sciences*, 1962, 3, 93-97.

The effects of α-methyl DOPA, 3-hydroxybenzyloxyamine (NSD 1024) and N-(3-hydroxybenzyl)-N-methylhydrazine (NSD

1034) on 5HTP decarboxylase were studied in vivo and in vitro. In the first experiments, the minimum effective doses necessary to prevent the characteristic tremors following administration of 5HTP (75 mg/kg) were determined in mice pretreated 2 hours before with the MAO inhibitor N-(1-methyl-2-phenoxyethyl)-hydrazine (5 mg/kg i. p.). In later experiments, the 5HTP decarboxylase activity of mouse brain homogenates was compared in treated animals and untreated controls; again, the amounts necessary to produce 50% and 80% inhibition of decarboxylase activity were determined. All 3 drugs were found to be powerful inhibitors of 5HTP decarboxylase in vivo and in vitro. As previously reported, α -methyl DOPA (400 mg/kg s. c.) also produces a marked decrease in the mouse brain 5HT level. In the case of NSD 1024, however, doses up to 64 mg/kg produced only a transitory decrease in 5HT, the level returning to normal long before the decarboxylase activity. It is therefore unlikely that the effect of α -methyl DOPA on cerebral 5HT is mediated wholly via inhibition of 5HTP decarboxylase.

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Great Britain

1573 Izquierdo, Juan A., Coussio, Jorge D., & Kaumann, Alberto J. Effect of imipramine on the pressor responses to the afferent vagal stimulation in reserpinized dogs. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 135, 303-310.

The effect of levarterenol ($0.5-2.0 \mu\text{g/kg}$), epinephrine ($1-2 \mu\text{g/kg}$) and imipramine ($3-10 \text{mg/kg}$) injected into the external iliac vein on the pressor response to afferent vagal stimulation was studied in anesthetized dogs (pentobarbital, 35 mg/kg) given reserpine (250 mg/kg) 1-48 hours earlier. Imipramine was found to oppose reserpine-induced hypotension, antagonizing the depressor response to vagal stimulation and, 1 hour but not 48 hours after reserpine, transforming it into a pressor response. Imipramine accentuated the magnitude and

duration of the pressor effect of levarterenol and, to a lesser extent, epinephrine. The lack of transformation in the depressor reflex 48 hours after reserpine was probably due to the depletion of catecholamines.

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Buenos Aires, Argentina

1574 Herz, Albert. "Über die Wirkung der optischen Isomere atropinartiger Substanzen auf das Zentralnervensystem. [Effect of the optical isomers of atropine-like substances on the central nervous system.] *Archiv für Experimentelle Pathologie und Pharmacologie*, 1962, 242, 508-521.

Extensive studies on mice, rats and rabbits showed that the central effects of the levorotatory forms of 3 atropine-like substances (hyoscyamine, Win 12085 and BS 6534) on motility, the response to arecoline (4 mg/kg morphine anesthesia and the EEG were much stronger than those of the dextrorotatory isomers. In the motility studies, the mice were pretreated with amphetamine (1 mg/kg). Even the levorotatory form of BS 6534 was ineffective in potentiating morphine (30 mg/kg) in rats. This difference between dextro- and levo- forms in central effects paralleled the difference in mydriatic effect on the mouse pupil, the ratio of effectiveness of the 2 isomers being in the range 0.01-0.08 in most cases. This indicates that cholinceptive mechanisms may play a role in central effects.

Pharmakologisches Institut
Universität München
Munich, Germany

1575 Bonta, I. L., Wijmenga, H. G., & Hohensee, F. Über die Wirkung von Substanz P und anderen Hirnextrakten auf das Zentralnervensystem. [Effect of substance P and other cerebral extracts on the central nervous system.] *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 10, 114-118.

Crude preparations of substance P from pig brain had a depressant effect on the central nervous system in doses of 1-6g/kg as shown by decreased exploratory behavior

in mice and the prevention of convulsions due to i.v. strychnine. There was no potentiation, however, of either hexobarbital anesthesia or morphine analgesia. Other pig cerebral extracts not containing substance P (as shown by tests on isolated, atropinized, guinea pig ileum) also had central nervous system depressant properties.

Pharmacological Research Department
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The Netherlands

1576 Femmer, K. Antitremorin-Wirkung von quaternären Phenothiazinbasen. [Antitremorine activity of quaternary phenothiazine bases.] *Arzneimittel-Forschung*, 1962, 12, 706-707.

Comparative studies in mice and cats showed that both Wu 2505 (N-2-dimethylethylammonium-2-methylethylphenothiazine ethosulfate) and Wu 2506 (N-2-dimethylethylammonium-1-methylethylphenothiazine ethosulfate) in doses of 5 mg/kg i.p. had a powerful and long-lasting anti-tremorine effect, as shown by the rotating-rod test and the hot-plate analgesia test in mice and tremorine-rage in cats; the effect of ethopropazine (5 mg/kg i.p.) was much more transitory. Both Wu 2505 and Wu 2506 also had significant anticholinergic activity on the isolated guinea pig ileum. This indicates that the anti-tremorine activity must be central in nature.

Forschungsabteilung I
VEB Arzneimittelwerk
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1577 Stock, K., & Westermann, E. Untersuchungen über den Mechanismus der narkoseverkürzenden Wirkung von Monoaminoxidase-Hemmstoffen. [Studies on the mechanism of the analeptic effect of monoamineoxidase inhibitors.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 44-64.

Measurements of the duration of hexobarbital (100 mg/kg i.p.) narcosis and of the cerebral catecholamine levels and MAO activity in male mice pretreated with

various MAO inhibitors and sedatives showed that the hydrazine MAO inhibitors iproniazid (100 mg/kg s.c.), nialamide (20 mg/kg s.c.) and JB 807 (benzylisopropylisopropylhydrazine; 20 mg/kg s.c.) prolonged hexobarbital anesthesia when given 1-6 hours earlier, but shortened it when given 20-48 hours before. The non-hydrazine MAO inhibitors pargyline (20 mg/kg s.c.) and tranlycypromine (10 mg/kg s.c.) shortened hexobarbital anesthesia when given 1-6 hours before, as did chlorpromazine (5 mg/kg s.c.) and SKF 525 A (diethylaminoethyl-diphenylpropylacetate; 50 mg/kg s.c.) given 20-48 hours earlier. The cerebral serotonin level was increased by all MAO inhibitors, but the shortening of anesthesia 20-24 hours after iproniazid or nialamide still persisted when the increase in brain serotonin was prevented by harmaline (30 mg/kg s.c.). Hexobarbital catabolism by liver microsomes was strongly inhibited 1-6 hours after the hydrazine derivatives, but activated 48 hours after treatment. Neither the nonhydrazine MAO inhibitors nor chlorpromazine or SKF 525 A had any significant effect, but phenobarbital (100 mg/kg s.c.) also shortened the duration of hexobarbital anesthesia and stimulated its catabolism. Iproniazid, SKF 525 A or phenobarbital also decreased the hexobarbital concentration found in the brain after injection. Thus the shortening of hexobarbital sleeping time by various agents is due to different mechanisms of action.

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Frankfurt, Germany

1578 Fink, Gregory B., & Swinyard, Ewart A. Comparison of anticonvulsant and psychopharmacologic drugs. *Journal of Pharmaceutical Sciences*, 1962, 51, 548-551.

Four anticonvulsant drugs and 7 tranquilizers were tested in male CFl mice for their ability to increase hexobarbital sleeping time, abolish CAR's and reduce amphetamine toxicity in mice aggregated 3 per cage (more severe test) and 10 per cage (less severe test). All drugs were used at

equitoxic doses, e.g., phenobarbital 70 mg/kg. Except for the 3 phenothiazine derivatives, all the drugs were ineffective in nontoxic doses in the 3 mice per cage test, while only phenobarbital, trimethadione, meprobamate and phenaglycodol were ineffective as measured by the 10 mice per cage test. Chlorpromazine, promazine and triflupromazine effectively reduced amphetamine toxicity in both situations. The phenothiazines, reserpine and hydroxyzine were active in the 10 per cage test; diphenylhydantoin and phenacemide were also effective which suggests that they have some tranquilizing properties. All drugs increased hexobarbital sleeping time. Chlorpromazine, promazine, triflupromazine, reserpine and hydroxyzine blocked CAR's and/or secondary conditioned responses. Meprobamate, phenaglycodol and the anticonvulsant drugs (diphenylhydantoin, phenacemide, phenobarbital and trimethadione) had little effect on CAR's in nontoxic doses.

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Salt Lake City, Utah

1579 Noach, E. L., Bunk, J. Joosting, & Wijling, A. Influence of electroshock and phenobarbital on nucleic acid content of rat brain cortex. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 54-69.

Studies were made in female rats to determine whether maximal electroshock evokes a decrease in brain nucleic acid, as reported for other species, and whether this decrease can be prevented with barbiturates in nonanesthetic, anticonvulsant doses. In addition, animals were housed either individually or in groups. Nucleic acids were estimated chemically (chromatography and spectrophotometry) in cerebral cortex slices from untreated controls, rats sacrificed 30-75 seconds after maximal electroshock, rats sacrificed 75 minutes after 15 mg phenobarbital, and rats sacrificed 30-75 seconds following maximal electroshock 75 minutes after 15 mg phenobarbital. No significant changes were observed in either amount or composition of DNA or RNA base composition. However, total RNA varied in 2 ways: in animals housed

together, the average cortical RNA level was lower than in animals kept in individual cages. In those housed separately a significant drop in RNA concentration was caused by maximal electroshock in phenobarbital-pretreated animals resulting in a suggestive increase in total RNA, as compared to unshocked, barbiturate-pretreated animals. Assuming a very rapid RNA turnover in the brain cortex, a rapid decrease (caused by maximal electroshock in unmedicated animals) may be due to an inhibition of RNA-biosynthesis or to an enhancement of its catabolism or decrease might be explained by an increase in both formation and breakdown of RNA with a slight predominance in breakdown. Also, electroshock after phenobarbital gives rise to an increase in RNA-turnover, synthesis being slightly predominant under these circumstances. This indicates that phenobarbital pretreatment inhibits RNA-breakdown in electrically shocked animals.

Department of Pharmacology
University of Leiden
Leiden, The Netherlands

1580 Griesemer, Ernest C., Gasner, Linda T., Clark, William G. Antagonism of reserpine hypothermia in mice by 3, 4-dihydroxyphenylalanine (DOPA). *Proceedings of the Western Pharmacology Society*, 1962, 5, 7-8.

Reserpine (7 mg/kg i.p.) administered to mice produced a continuous prolonged decline in rectal temperature which remained consistently reduced for over 7 hours and was unaltered by administration of iproniazid 1 hour after reserpine. DOPA produced a temperature rise in normal and reserpinized mice which was markedly potentiated by iproniazid. Pargyline produced an equivalent potentiation of this response. Adrenergic blocking agents blocked the temperature rise. Two ergot derivatives, dichlorisoprotenerol and atropine failed to block the rise, but it was potentiated by cocaine. The increase in temperature is apparently precipitated by conversion of DOPA to catecholamines. This effect may be mediated in the central temperature regulating mechanism and may be correlated with increased activity in the brain arousal centers.

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1581 Smith, Con L., & Robinson, Willaim A.
The effect of diphenylhydantoin sodium on liver
restitution in the rat following hepatectomy.
Proceedings of the Western Pharmacology
Society, 1962, 5, 9-12.

Rats received diphenylhydantoin (10 mg/day
i.p. for 10 days before and 5 days after
hepatectomy or 10 mg/day i.p. for 5 days
after hepatectomy), 0.1 cc of commercial
diluent or nothing. Animals were sacrificed
0-5 days postoperatively and their livers
examined histologically. The amount of liver
tissue restitution in diphenylhydantoin-
treated animals was significantly greater in
all groups from days 2-5. The drug exerted
no significant proliferative effect upon the
liver before hepatectomy. Animals receiv-
ing only diluent showed no significant dif-
ference from controls at the end of a 5-day
period of restitution, nor did those who re-
ceived diphenylhydantoin only after hepa-
tectomy. Animals pretreated with diphenyl-
hydantoin prior to hepatectomy exhibited
significant increases in hepatic parenchy-
mal tissue.

Department of Pharmacology
University of Colorado School of Medicine
Denver, Colo.

1582 Mackay, Frances, & Cooper, Jack R.
Hypnotic activity of chloral hydrate.
Anesthesiology, 1962, 23, 155.

In an attempt to correlate the degree of
neurological depression with the levels of
chloral hydrate and trichloroethanol in the
brain, mice were given 0.4 mg/g chloral
hydrate i.p. The animals were sacrificed
at different time intervals and the brains
analyzed for chloral hydrate and trichloro-
ethanol. The injections caused the loss of
the righting reflex in 7-32 seconds. At this
time the chloral hydrate concentration was
283 μ g/g brain and the trichloroethanol con-
centration only 31.1 μ g/g brain. Another
group of mice was given 0.04 mg/g trichloro-
ethanol i.v. and sacrificed 10 seconds later.
Although these mice showed no signs of
sedation, the average concentration of tri-

chloroethanol was 86.3 μ g/g brain. There-
fore the hypnosis observed in the mice
given chloral hydrate i.v. must have been
produced by the chloral hydrate itself rather
than by trichloroethanol.

Section of Anesthesiology
Yale University School of Medicine
New Haven, Conn.

1583 Sudak, Frederick N., Essman,
Walter B., & Hamburg, Max. Anticonvuls-
ive effects of 2,4-dichlorophenoxyacetic
acid in mice susceptible to audiogenic seiz-
ures. Experimental Neurology, 1962, 6, 30-
35.

The anticonvulsive effects of 2,4-dichloro-
phenoxyacetic acid were investigated in Swiss
mice predisposed to audiogenic seizures.
In 1 experiment 2,4-dichlorophenoxyacetic
acid was given i.p., 25-150 mg/kg, to 56
animals, while 11 controls received saline;
all were then tested for seizures 30 minutes
postinjection. The ED₁₀₀ was 100 mg/kg and
the ED₅₀ was 75 mg/kg, well below the LD₅₀
of 375 mg/kg reported by Hill and Carlisle
(1947). The duration of protection was
investigated in a 2nd experiment with 38 mice
tested 24-72 hours after receiving 2,4-di-
chlorophenoxyacetic acid. In a 3rd experi-
ment, the time of onset of the protective
effect of 2,4-dichlorophenoxyacetic acid,
100 mg/kg i.p., was determined. Animals
were protected against audiogenic seizures
by 100-150 mg/kg of 2,4-dichlorophenoxy-
acetic acid; an increase in latency period
occurred in mice treated with 50-75 mg/kg.
The onset of protection by 100 mg/kg
occurred after 5 minutes, with complete
protection ensuing within 15 minutes; pro-
tection lasted for 24, but not 48 hours.

Department of Physiology
Albert Einstein College of Medicine
New York, N. Y.

1584 Kugita, Hiroshi., Saito, Seichi., &
May, Everette L. Structures related to
morphine. XXII. A benzomorphan congener
of meperidine. Journal of Medicinal and
Pharmaceutical Chemistry, 1962, 5, 357-
361.

The synthesis and chemistry of 5-carbethoxy-2-methyl-6,7-benzomorphan, essentially a hybrid of benzomorphan and meperidine, was described. Its s.c. analgesic activity (ED₅₀ 10.0 mg/kg) was determined by the procedure of Eddy and Leimbach and found to be comparable to meperidine (ED₅₀ 9.9 mg/kg). The amide was about half as potent (ED₅₀ 18.1 mg/kg) and the amine quite inactive.

Laboratory of Chemistry
NIH
Bethesda, 14, Md.

1585 Gaines, Thomas B. Poisoning by organic phosphorus pesticides potentiated by phenothiazine derivatives. *Science*, 1962, 138, 1260-1261.

Sherman rats received parathion (5 ml/kg intragastrically) followed by promazine and chlorpromazine (0.8 ml/kg intragastrically or i.p.) after which LD₅₀ values were calculated by the method of Hitchfield and Wilcoxon. Groups of male rats received 1 oral dose of parathion (3-15 mg/kg) followed by oral doses of promazine or chlorpromazine (both 3 mg/kg). Treatment with promazine increased the toxicity of parathion by a factor of 2 and chlorpromazine increased it to a lesser degree. Administration of these drugs to parathion-poisoned rats altered neither the time of onset of symptoms nor the time of death. Male rats treated with promazine (up to 160 mg/kg) or chlorpromazine alone exhibited marked depression but recovered overnight upon drug withdrawal. Promazine (15 mg/kg) potentiated the toxicity of parathion (2.5 mg/kg) when administered to groups of 10 female rats within 30 minutes before or up to 1 hour after parathion. Minimal effects ensued with promazine given 4 hours after parathion. Groups of 10 female rats received promazine (50 mg/kg p.o.) 30 minutes before, at the same time, and at 2 intervals after a 13 mg/kg dose of Phosdrin. Promazine had no effect upon Phosdrin, all rats exhibiting typical symptoms of Phosdrin poisoning. In treating parathion or Phosdrin poisoning, phenothiazine derivatives should be avoided or utilized with extreme caution.

Toxicology Section
CDC
Atlanta 22, Ga.

1586 Shapiro, Seymour L., Parrino, Vincent A., Isaacs, Elaine S., & Freedman, Louis. Indanols. IV. Indanoxypropanolamines. *Journal of Medical and Pharmaceutical Chemistry*, 1962, 5, 69-76.

A series of indanoxypropanolamines were evaluated as CNS depressants, and related compounds were evaluated as analgesics, hypnotics, anticonvulsants and muscle relaxants. The Muscle Relaxant Test and Audiogenic Seizure Test were used, as well as determinations of the lethal dose, analgesic and antitremorine effects and effect on spontaneous motility. The best muscle relaxant activity was obtained in ROCH₂CHOHCH₂A compounds wherein R is 4-indanyl and A is a relatively weakly basic secondary amino group.

Research Laboratories
U. S. Vitamin & Pharmaceutical Corporation
Yonkers, N. Y.

1587 Polis, David B. Increase in acceleration tolerance of the rat by 2-dimethylaminoethyl P-chlorophenylacetate (Lucidril). *Aerospace Medicine*, 1962, 33, 930-934.

Previous studies on centrophenoxine (Lucidril) which suggested involvement of the pituitary adrenal axis as well as the hypothalamic area of the brain led to this investigation of its effect on acceleration tolerance. Male Sprague Dawley rats, were given i.p. 5% Lucidril. A control group was given physiological saline. Tolerance to acceleration stress was evaluated using a small animal centrifuge and end point for acceleration tolerance determined by following the ECG (Sipple and Polis 1961). Tolerance to acceleration was significantly enhanced at 20 gravities. Median survival time of treated animals increased to 33.3 minutes compared to control survival time of 12.5 minutes. The effectiveness of the drug persisted for 4

hours after injection. Prior to apparent enhanced tolerance, a latent period of 3-4 days of drug treatment was necessary. Activity was dose-dependent. No significant changes in acceleration tolerance were found with a total injection of 50 mg, significant increments in tolerance were obtained with 75 mg and much larger increases in tolerance to acceleration followed administration of 100 mg. Centrophenoxine is probably mediated via the hypothalamic area, possibly by interplay with the biogenic amines. Its structural relationship to acetylcholine suggests additional areas for investigation of the mechanism of its action and also for the investigation of the role of this hormone in acceleration stress tolerance. As it has low toxicity and has already been used by humans in high doses, centrophenoxine may be effective in increasing human tolerance to acceleration.

Aviation Medical Acceleration Laboratory
U.S. Naval Air Development Center
Johnsville, Pa.

1588 Locker, A., & Ellegast, H. Librium als Strahlenschutzsubstanz für Mäuse. [Librium as a radioprotective agent in mice.] *Experientia*, 1962, 18, 363-364.

Male mice were subjected to total body X-ray dosages of 800 r (at the rate of 40 r/minute), 15 minutes after the injection of varying doses of chlordiazepoxide (Librium). The effective range for chlordiazepoxide was found to be very narrow, between 7.5 and 12.5 mg/kg. The chi-square test shows that the increase in survival rate in this range is statistically significant at the 0.05 probability level.

Institut für Biologie und Landwirtschaft
Reaktorzentrum Seibersdorf-Wien
Vienna, Austria

1589 Zbinden, Gerhard. Beeinflussung der experimentellen, durch Isoproterenol hervorgerufenen Myocardnekrose durch Aminoxydasehemmer, gefässerweiternde und tranquilisierende Arzneimittel. [Influence of amineoxidase inhibitors, vasodilators and tranquilizers on isoproterenol-induced myocardial necroses.] *Arzneimittel-Forschung*, 1962, 12, 635-638.

Isoproterenol (0.2-80.0 mg/kg s.c.) was injected into 597 rats and the influence of pretreatment with a number of drugs on the resulting infarct-like myocardial necroses was measured. Coronary dilators like sodium nitrite, aminophyllin, and dipyridamol, sedatives like reserpine, chlordiazepoxide, chlorpromazine, meprobamate, and adrenolytics like azapetine, did not affect the myocardial necroses. Aminoxydase inhibitors like iproniazid, isocarboxazid, and pivalylbenzylhydrazine significantly inhibited the isoproterenol necroses. Aminoguanidine and tranilcypromine were also ineffective. Calculation of significance levels was performed by the Fisher-Yates method.

Hoffmann-LaRoche, Inc.
Department of Biological Research
Nutley, N.J.

1590 Wulfsohn, N.L., & Politzer, W.M. 5-Hydroxytryptamine in anaesthesia. *Anaesthesia*, 1962, 17, 64-68.

Mice were anesthetized with ether, chloroform or halothane to the point of narcosis. The drugs administered i.p. were: a/ 2.5 mg/kg 5HT, b/ drugs which increase 5HT level-100 mg/kg iproniazid, 5 mg/kg reserpine and 5 mg/kg tetrabenazine and c/ 5HT blocking agents-5 mg/kg methysergide, 0.1 mg/kg lysergide and 0.3 mg/kg hydergine. The duration of sleep was taken as the time required for the mice to right themselves. Sleeping time following general anesthesia is generally prolonged by 5HT and MAO inhibitors, while not necessarily shortened by 5HT blocking drugs. 5-Hydroxytryptamine causes an increase of respiratory rate which can be reduced by methysergide. 5-Hydroxy-indole acetic acid is not increased following anesthesia. The possibility of prolonging sleeping time in psychiatric patients receiving MAO inhibitors when administering general anesthetics should be accounted for.

South African Institute for Medical
Research
Johannesburg, Union of South Africa

1591 Haeger-Aronsen, Birgitta. Porphyrin induced in the rabbit by diethyl-1, 4-dihydro-2, 4, 6-trimethylpyridine-3, 5-dicarboxylate. II. Catalase activity and concentration of green porphyrins in the liver and a comparison with apronal-induced porphyria. *Acta Pharmacologica et Toxicologica*, 1962, 19, 156-164.

Hepatic porphyria was induced in 56 rabbits by administering p.o. 200 mg/kg of diethyl-1, 4-dihydro-2, 4, 6-trimethylpyridine-3, 5-dicarboxylate to 15 rabbits and the results were compared to those obtained in 9 rabbits with apronalide (apronal; 100-400 mg/kg p.o.). Four rabbits received only 10 ml of 96% ethanol (the vehicle). Urine and feces were analyzed during the period of drug treatment; animals were then sacrificed. Both drugs gave similar results; a substantial reduction in liver catalase and increase in green porphyrins, increased urinary excretion of 5-aminolevulinic acid, porphobilinogen, uroporphyrin and coproporphyrin and increased fecal coproporphyrin and protoporphyrin. The metabolic block induced is assumed to be the same in these 2 types of porphyria.

Department of Clinical Chemistry
University of Lund
Malmö, Sweden

1592 Funcke, A.B.H., De Jonge, M.C., Tersteeg, H.M., Mulder, D., Harms, A.F., & Nauta, W.Th. Preliminary communication; Pharmacological properties of 3-(10, 11-dihydro-5H-dibenzo [a, d] cyclohepten-5-yloxy) -tropane citrate (BS 6987, dibenzheptropine citrate). *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 104-112.

Dibenzheptropine citrate (BS 6987) was tested for: acute toxicity (mice, rats and dogs); chronic and subacute toxicity (rats); local tissue irritation (rabbits); antihistamine activity (guinea pig intestine, narcotized cat, guinea pigs); antiserotonin activity (isolated rat uterus, narcotized cat, rat hind paw, guinea pigs); cholinergic action (isolated guinea pig intestine, narcotized cat, guinea pigs); spasmolytic

action (isolated guinea pig intestine); adrenolytic action; antisecretory activity (alcohol-stimulated gastric juice secretion in dogs, histamine-induced secretion in the cat, gastric ulcers in the starved and cold-stressed rat, salivary flow in rabbits); mydriatic action (mice and dogs); CNS action (mouse, guinea pig, rat). BS 6987 was found to be decidedly active against experimental bronchospasms, both after parenteral and oral administration. Its strong peripheral histaminolytic and cholinergic activities play a part in this effect. In contrast to its marked peripheral actions, central effects were of minor importance, which makes it likely that it would be therapeutically active in patients suffering from asthmatic diseases, chronic bronchitis, rhinitis, etc.

Research Department N. V. Koninklijke
Pharmaceutische Fabrieken
v/h Brocades Stheeman en Pharmacia
Amsterdam, The Netherlands

1593 Zarrow, M.S., Pawlowski, A.A., & Denenberg, V.H. Electroshock convulsion threshold and organ weights in rats after alcohol consumption. *American Journal of Physiology*, 1962, 203, 197-200.

The effect of ethyl alcohol (5-10% as the only drinking fluid for 141-157 days) was compared with that of stress (daily i.p. injection of 0.1 cc 1.5% aqueous formaldehyde) in 137 Wistar rats. Thresholds for both the minimal and maximal seizure were determined. In the minimal seizure experiment, values were 21.4 ma for the control group and 25.7 for 10% alcohol-treated rats; in maximal seizure groups, the average threshold was 34.3 ma for the control group, 48.2 ma for the 10% alcohol-treated group, 39.5 ma for the 5% alcohol-treated group and 29.8 ma for the formaldehyde-stressed group. In both instances the threshold elevation was statistically significant at the 1% level. Postmortem examination revealed no significant changes in the liver or endocrine system, and it was concluded that the increased electroshock convulsion threshold after chronic alcohol consumption is probably due to a CNS depressant action

of alcohol.

Department of Biological Science
Purdue University
Lafayette, Ind.

1594 Wolf, Harold H., Swinyard, Ewart A., & Goodman, Louis S. Anticonvulsant properties of some N-substituted hydantoins. *Journal of Pharmaceutical Sciences*, 1962, 51, 74-76.

The anticonvulsant potencies (ED_{50} 's) of 3 N-substituted hydantoins, 1-methyl-5,5-phenylethylhydantoin (compound I), 1,3-dimethyl-5,5-phenylethylhydantoin (II), and 3-ethyl-5,5-phenylethylhydantoin (III), and of phenantoin and diphenylhydantoin were determined in mice by the following 3 tests: maximal electroshock seizure pattern (MES) test, low-frequency electroshock seizure threshold (l.f. EST) test, and pentylenetetrazol seizure threshold (s.c. Met.) test. In addition, neurotoxicity (TD_{50} 's) was determined and the protective index ($P.I. = TD_{50}/ED_{50}$) was calculated. The TD_{50} 's for the 3 experimental drugs were significantly higher than those for phenantoin and diphenylhydantoin. The N-substituted compounds showed activity in all 3 tests; however, except for diphenylhydantoin by the s.c. Met. test and (II) by the l.f. EST test, they were less potent than the 2 clinically employed agents. (I) was more effective in elevating the seizure threshold than in modifying the maximal seizure pattern, whereas diphenylhydantoin was more effective in modifying the maximal seizure pattern. (II), (III), and phenantoin showed no striking selectivity of action. On the basis of P.I.'s, (I) appears to be the most promising of the 3 experimental drugs. Structure-activity studies indicated that mono-methyl substitution on a nitrogen of the hydantoin ring exerted a more favorable influence on anticonvulsant activity than either di-methyl or mono-ethyl substitution and that optimal activity was obtained when the methyl substitution was on the nitrogen in position 3 of the hydantoin ring.

College of Pharmacy and College of Medicine
University of Utah
Salt Lake City, Utah

1595 Courville, Jacques, Walsh, John, & Cordeau, J. Pierre. Functional organization of the brain stem reticular formation and sensory input. *Science*, 1962, 138, 973-975.

Small quantities of epinephrine, acetylcholine or procaine were injected slowly, directly into the brain stem reticular formation of unanesthetized encephale isolé cats, of cats immobilized with gallamine, and single-shock, square-wave pulses were delivered to the optic chiasma at a frequency of 1 pulse every 3 seconds; the evoked potential, recorded from the visual cortex of the posterolateral gyrus, was displayed on a cathode-ray oscillograph. Injection of $20\mu g$ epinephrine was followed by a transient increase in the amplitude of the cortical-evoked response while injections of the same amount of acetylcholine produced a transient decrease. Injection of procaine into the medial region of the rostral pontine reticular formation was followed by a long-lasting increase in the amplitude of these evoked responses, while the same injections at mesencephalic levels produced a marked decrease. The reticular formation must contain 2 antagonistic ascending systems: 1 adrenergic, the other cholinergic, whose tonic activity originates in the mesencephalic tegmentum in 1 case and the caudal regions of the brain stem in the other.

Department of Physiology
University of Montreal
Montreal, Quebec
Canada

1596 Sidhu, G.S., Sattur, P.B., & Jaleel, Salma. Synthesis and anticonvulsant activity of some N-phenethylacetamides. *Journal of Pharmacy and Pharmacology*, 1962, 14, 125.

Two out of 5 chloroacetamides synthesized had anticonvulsant activity. Rats were given maximal electroshock seizures from corneal electrodes. α -Chloro-N-phenethylacetamide (I) was the most active and its anticonvulsant activity was compared to phenobarbital, phenytoin and troxidone. The ED_{50} of these compounds administered orally was 5 mg/kg for (I), phenobarbital

and phenytoin, and 100 mg/kg for troxidone. The percentage of protection by oral doses of 5, 10 and 15 mg/kg of the acetamide was 64, 80 and 96, while corresponding figures for phenobarbital were 48, 76 and 96; for phenytoin 52, 64 and 76; for troxidone 52, 64 and 72. The Peak Effect was found at 4, 3, 4 and 2 hours respectively. Another compound, α -chloro-N-m-chlorophenethylacetamide was about two-thirds as potent as (I). The 3 other compounds synthesized showed no significant anticonvulsant activity and none of the compounds protected against leptazol-induced seizures.

Regional Research Laboratory
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1597 Von Euler, U.S., & Lishajko, F. Release and uptake of catecholamines in nerve storage granules in relation to adrenergic neuro-transmission. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 276-280.

Studies with sedimented bovine splenic nerve granules showed that the liberation of levarterenol into isotonic phosphate buffer could be prevented by addition of levarterenol to the medium at concentrations of 10 μ g/ml. Previously depleted granules took up added levarterenol from the medium at a rapid rate, and added epinephrine was taken up even without prior depletion. Some conclusions are drawn with regard to the process of transmitter release in vivo.

Department of Physiology
Faculty of Medicine
Karolinska Institute
Stockholm, Sweden

1598 Herz, Albert. Wirkungen des Arecolins auf das Zentralnervensystem. [Effects of arecoline on the central nervous system.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 242, 414-429.

In rats, s.c. injections of arecoline increased motor restlessness and had a marked analgesic effect in doses (1-2 mg/kg)

at which no peripheral muscarinic effects could be observed. The analgesic effect was practically abolished by atropine, scopolamine (1 mg/kg), trihexyphenidyl and benactyzine (5-20 mg/kg), but not by antinicotinic drugs. Arecoline (2 mg/kg) also inhibited CAR's in rats. In comparable experiments with morphine (7.5 mg/kg i.p.) the analgesic effect was potentiated by benactyzine and trihexyphenidyl, while scopolamine had no effect in this test but potentiated the inhibitory effect of morphine on CAR's. Similar results were obtained with arecoline (4 mg/kg s.c.) in mice. In rats, s.c. injections of 1-2 mg/kg produced a drop in blood pressure of 10-40 mm Hg, beginning 1 minute after the injection and lasting 2-5 minutes; this response was abolished by atropine.

Pharmakologisches Institut der
Universität München
Munich, Germany

1599 Lang, W., & Gershon, S. Effects of psychoactive drugs on yohimbine induced responses in conscious dogs. A study of depressant drugs. *Medicina Experimentalis* 1962, 7, 125-134.

Dogs were surgically prepared with exteriorized carotid arteries in skin loops and trained to remain in a Pavlov-type stand and harness. The ECT, continuous blood pressure directly from the carotid and heart rate were recorded. An undwelling cannula in the jugular was used for all injections. Yohimbine was injected at 0.1 and 0.5 mg/kg; 2.5 mg/kg imipramine, 1.5 mg/kg amitriptyline, 1.5 mg/kg nortriptyline, 1-3 mg/kg nialamide and 2.5 mg/kg iminostilbene were administered. Also 10 mg/kg chlorpromazine was given orally to some dogs for 3 weeks. Imipramine, amitriptyline, nortriptyline and nialamide potentiated the "anxiety-like state" produced by yohimbine. Chronic medication with chlorpromazine potentiated both an increase in blood pressure and heart rate induced by yohimbine. This contrasts to inhibition of yohimbine response in acute experiments with chlorpromazine.

Department of Pharmacology
University of Melbourne
Melbourne, Australia

1600 Pletscher, A. Basic aspects of psychotropic drug action. *American Journal of Mental Deficiency*, 1962, 67, 238-244.

With respect to the mechanism of action of psychotropic drugs affecting cerebral monoamines, rauwolfia alkaloids and benzoquinolizine derivatives with sedative action, reserpine and tetrabenazine, respectively, cause a marked decrease in cerebral 5HT, levarterenol and dopamine with concomitant increase in their urinary metabolites. Monoamine synthesis is blocked by the administration of α -methyl dopa or α -methyl 5HTP which cause a decrease of 5HT, levarterenol or dopamine in brain tissue due to decarboxylase inhibition. Repeated administration of inhibitors results in sedation. These drugs also release endogenous monoamines either by displacement or by impairing the storage capacity of brain tissue. MAO inhibitors (irreversible effects: hydrazine derivatives such as iproniazid, pheniprazine, phenelzine, etc.; reversible effects: harmaline derivatives such as harmine or harmaline) produce rapid or sustained increases in endogenous monoamines in brain tissue due to drug-induced inhibition of monoamine degradation of 5HTP, dopa, etc., which produce marked CNS stimulation due to inhibition of MAO with accumulation of monoamines. Certain phenothiazines and thioxanthenes may inhibit penetration of monoamine through biological membranes. Chlorpromazine and chlorprothixene decrease the permeability of stored monoamine particles (stored in biologically inactive form), thus diminishing the degree of monoamine release by reserpine. A reduction in storage precedes metabolic inactivation of newly formed monoamines. Hypothetically, psychostimulating effects from thymoleptic drugs like imipramine and amitriptyline may be derived from enhancement of the sensitivity of cerebral synapses for monoamines. Numerous experiments are mentioned which corroborate the above mechanisms as causative factors for the pharmacodynamic and clinical effects of psychotropic drugs.

Medical Research Department
F. Hoffmann-La Roche and Co., Ltd.
Basel, Switzerland

1601 Ayala, G.F. Un metodo per l'iniezione di farmaci in aree limitate del cervello del coniglio. [A method for the injection of drugs into a limited area of the rabbit brain.] *Bollettino della Società Italiana di Biologia Sperimentale*, 1962, 38, 157-160.

A surgical technique for localizing drugs to the cerebral circulation following injection into the subclavian artery, involving ligation of the basilar, external carotid, thyrocervical trunk and internal mammary arteries, insertion of a by-pass into the common carotid, and temporary clamping of the subclavian artery following injection so that the drug ascends the vertebral artery, is described in detail. The effectiveness of the technique was tested by injection of Monastral-blue, and it was confirmed that ligation of the basilar artery at the level of the pons per se and the injection of saline had no significant effect on the EEG.

Reparto Neurochirurgico
Ospedale Civico e Benfratelli
Palermo, Italy

1602 Pletscher, A., Besendorf, H., Steiner, F. A. & Gey, K. F. The effect of 2-hydroxy-benzoquinolizines on cerebral 5-hydroxytryptamine, spontaneous locomotor activity, and ethanol hypnosis in mice. *Medicina Experimentalis*, 1962, 7, 15-20

Mice received injections of 7 newly synthesized 2-hydroxy-hexahydro-benzo [a] quinolizines (5-50 mg/kg i.p. or s.c.) after which the following measurements were made: 5HT in total brain by spectrophotofluorometry, spontaneous locomotor activity by a modified photographic method and ethanol potentiation (drug treated mice received ethanol (4 g/kg i.p.) prior to measurement of sleeping time). No strict correlation could be established between diminution of cerebral 5HT and reduction of spontaneous locomotor activity or ethanol potentiation. All 7 derivatives decreased motor activity and potentiated the effect of subhypnotic doses of ethanol, but only 4 compounds decreased brain 5HT. Pretreatment with

iproniazid reversed the sedative action of 5HT lowering derivatives. Two different mechanisms may account for depression of locomotor activity, unrelated to monoamine metabolism, the other predicated upon monoamine release. It appears unlikely that 5HT release is a major factor in producing ethanol potentiation. The action of these compounds on brain amines apart from 5HT remains to be established. Preliminary results indicate that levarterenol behaves qualitatively like 5HT.

Medical Research Department
F. Hoffmann-La Roche & Co., Ltd.
Basel, Switzerland

1603 Bisson, Gabriele M.,) Muscholl, E. Die Wirkung von Guanethidin und Hexamethonium auf die Aufnahme zirkulierenden Noradrenalins in das Herz. [Effect of guanethidine and hexamethonium on the uptake of circulating levarterenol by the heart.] *Naturwissenschaften*, 1962, 49, 110.

Studies in spinal rats showed that the uptake of levarterenol (noradrenalin) by the heart following i.v. injection of 20 μ g was prevented by guanethidine (15 mg/kg i.v.) but not by hexamethonium (20 mg/kg i.v.) Guanethidine alone had little immediate effect on the levarterenol content of the heart, but depleted it almost completely in 20 hours.

Pharmakologisches Institut
Universität Mainz
Mainz, Germany

1604 Zábajniková, M., & Kovalčík, V. Analgetické účinky inhibitorů MAO. [Analgetic effects of MAO inhibitors.] *Ceskoslovenska Fysiologie*, 1962, 11, 537. [Abstract]

Studies in mice using the method of Siegmund et al. showed that trans-2-phenylcyclopropylamine (SKF 385B) had a marked analgesic effect (ED_{50} 2.6 mg/kg s.c. compared to 33 mg/kg for amidopyrine when given in combination. Thus, the ED_{50} of morphine was increased from 0.94 to 1.5 mg/kg s.c. by pretreatment with 1 mg/kg of SKF 385B, and that of

amidopyrine was increased from 26 to 35 mg/kg s.c. No ED_{50} within the limits of toxicity could be determined for SKF 385B, however, by the method of D'amour Smith.

Charles University Medical School
Bratislava, Czechoslovakia

1605 Hapke, H. J. Die Wirkungen von Narkotika, Analeptika, Secale-Präparaten und Phenothiazin-Derivaten auf vagale Atem- und Kreislaufreflexe bei Ratten und Meerschweinchen. [Effects of narcotics, analeptics, ergot alkaloids and phenothiazine derivatives on vagal respiratory and circulatory reflexes in rats and guinea pigs.] *Medicina Experimentalis*, 1962, 7, 77-84.

The response of the respiratory rate and carotid blood pressure to electrical stimulation of the vagus following administration of various drugs was studied in 49 rats and 53 guinea pigs under urethane (chloralose urethane or pentobarbital anesthesia). Barbiturates (5-10 mg/kg) and morphine (2 mg/kg) produced slight respiratory depression themselves and usually intensified the effect of vagal stimulation, resulting in respiratory arrest; there was little effect on blood pressure from the barbiturates, but morphine or methadone (0.5 mg/kg) potentiated the hypotensive effect of vagal stimulation. Pentetrazol (5-10 mg/kg) and bemegride (2-5 mg/kg) counteracted the respiratory effects of vagal stimulation, while ergot alkaloids had little effect. The effects of chlorpromazine (0.05-2.0 mg/kg) on the respiratory response to vagal stimulation were quite variable, while promethazine and propionylpromazine had no significant effect at 0.5-2.0 mg/kg; all 3 phenothiazines, however, as well as the ergot alkaloids, blocked the circulatory responses to vagal stimulation.

Pharmakologisches Institut der
Tierärztlichen Hochschule
Hannover, Germany

1606 Scocchera, Licia Fides. Un nuovo derivato fenotiazinico: la dixirazina. [A new phenothiazine derivative:

dixirazine.] *Clinica Terapeutica*, 1962, 23, 375-382.

After reviewing the structures of the phenothiazine and diphenylmethane derivatives and the initial attempts to combine their properties by synthesizing new compounds, the author reports extensive studies comparing the pharmacological properties of dixirazine, a new phenothiazine derivative containing the piperazine functional group of hydroxyzine, with those of promazine and chlorpromazine. The 3 drugs were found to be quite similar with respect to the potentiation of hexobarbitone narcosis in rats, the induction of hypotonic and catatonic states, the effects on behavior, motility, conditioned reflexes and amphetamine psychosis, and the antiapomorphine and antihistaminic properties, but dixirazine is less toxic. It was therefore tried clinically at doses of 20-75 mg/day with good preliminary results in gastrointestinal and cardiovascular conditions of neurotic origin, fever, pyloric spasm, vomiting, ulcerative colitis, asthma, insomnia, anxious depression and psychoneurosis.

No Address

1607 Delga, Jean, Laboure, Jacques & Olive, Georges. Etude de l'élimination et de quelques propriétés pharmacologiques du méprobamate et de trois de ses homologues. [A study of the elimination and some pharmacological properties of meprobamate and three of its homologues.] *Annales Pharmaceutiques Françaises*, 1962, 20, 121-126.

The effects and urinary excretion of meprobamate and the dicarbamates of ethylbutyl-, butylisopropyl- and butylisobutyl-propandiol-1,3 were compared in mice and rats. The water solubility and toxicity (LD_{50} i.p.) of the 4 compounds, as well as the hypnotic activity in mice (rotating rod test and potentiation of hexobarbital narcosis), were found to decrease in the order listed. Studies of the urinary excretion following administration of 200 mg/kg i.p. to rats showed that the rapidity of elimination also decreased in the same order, 80% of the meprobamate

and only 9-27% of the other drugs being excreted in 48 hours. Permeability factors or rate of diffusion thus seem to play a primary role.

Laboratoire de Chimie
Val-de-Grâce
Paris, France

1608 Floris, V., Morocutti, G. & Ayala, G. F. Azione della nicotina sulla attività bioelettrica della corteccia del talamo e dell'ippocampo nel coniglio. Sus azione di "arousal" e convulsivante primitiva sulle strutture ippocampo-talamiche. [Effect of nicotine on the bioelectric activity of the thalamic and hippocampal cortex in the rabbit. Its "arousal" and primary convulsant effects on the hippocampal-thalamic structures.] *Bollettino della Società Italiana di Biologia Sperimentale*, 1962, 38, 407-410.

The site of action of nicotine on the CNS was studied by recording the EEG in 15 rabbits, including 4 in which the brain was isolated by section of the cerebral trunk and 4 in which the cortex was deprived of afferent innervation. In the intact rabbit or the isolated rabbit brain, 1-2 mg/kg i.v. produced general activation of the EEG, while 2-6 mg/kg produced generalized convulsions; these seemed to originate in the hippocampus. In the isolated cortex nicotine had no effect, although caridazol still produced the typical convulsive phenomena. Nicotine thus seems to act preferentially on the cholinergic portion of the ascending meso-diencephalic activating system.

Clinica delle Malattie Nervose e Mentali
Università di Cagliari
Cagliari, Italy

1609 Quevauviller, André, Blanpin, Odette & Garet-Pottier, Janine. Pharmacodynamie de la raugalline, nouvel alcaloïde isolé du *Rauwolfia serpentina* Benth. Apocynacées. [Pharmacodynamics of raugalline, a new alkaloid isolated from *Rauwolfia serpentina* Benth. (Apocynaceae).] *Annales Pharmaceutiques Françaises*, 1962, 20, 19-21.

Studies of the acute i.v. toxicity in mice (LD_{50} = 33 mg/kg), the effect on smooth muscle (rat duodenum and guinea pig ileum) and isolated rabbit heart, and the hypotensive, antinicotinic and peristaltic effects in dogs indicated that raugalline may be indicated in cases of intestinal atonia in view of its mild parasympatholytic and sympatholytic properties.

Faculté de Pharmacie
Université de Paris
Paris, France

1610 Lecoq, Raoul, Chauchard, Paul & Mazoue, Henriette. Recherches chronaximétriques sur l'action qu'exercent quelques psycholeptiques et psychotoniques sur les effets nerveux de l'alcool éthylique. Conclusions pratiques. [Chronaximetric studies on the action of some psychotropic and psychotonic drugs on the neurological effects of ethyl alcohol. Practical conclusions.] Annales Pharmaceutiques Françaises, 1962, 20, 607-622.

Measurements of chronaxy in the flexor and extensor nerves of the toes in rats following i.p. injection of 37 different sedatives, tranquilizers, neuroleptics, energizers and psychotomimetics, along with experiments on the effect of these drugs on the metachronoses due to ocular compression, sharp noises or the injection of anterior pituitary extract, showed that these drugs can be classified into 3 groups; the specific depressants of the basal regulatory centers, such as chlorpromazine; the common hypnotics and general depressants, including reserpine; and agents such as meprobamate which uncouple the cerebral cortex from the periphery. The authors then studied the effect of these drugs on the response to i.p. ethyl alcohol, which usually has a diphasic effect consisting of diminution and then increase in neurochronaxy; this effect was suppressed by most of the drugs tested, but was accentuated by meprobamate, benactyzine, methylpentynol carbamate and reserpine. These results were confirmed by experiments with chronic administration of alcohol (1 ml/day for 5 days). Finally, when the psychotropic drugs were combined with disulfiram (0.5 ml 1% dispersion i.p.)

some of those previously showing protective effects no longer did so (vinylbarbital, isoamylethylmalonylurea, phenylbutazoline, chlordiazepoxide, methylpentynol carbamate, azacyclonol, prothipendyl, thioridazine, nialamide, imipramine, LSD and psilocybin).

Laboratoire du Centre Hospitalier
Saint-Germain-en-Laye, France

1611 Sicuteri, F., Michelacci, S. & Franchi, G. Contributo alla caratterizzazione della farmacologia della reserpina sul sistema nervoso centrale. Antagonismo di un bloccante adrenergico sul fenomeno della eccitazione paradossa da reserpina nel topo. [Contribution to the characterization of the pharmacological effect of reserpine on the central nervous system. Antagonistic effect of an adrenergic blocking agent on the paradoxical excitation due to reserpine in the mouse.] Bollettino della Società Italiana di Biologia Sperimentale, 1962, 38, 381-384.

Studies on the spontaneous motor activity of white mice showed that the usual motor excitation produced by reserpine (10 mg/kg) following pretreatment with iproniazid (200 mg/kg/day for 3 days) was completely prevented by the adrenergic blocking agent phentolamine (1 mg/kg), but was unaffected by the antiserotonin drug UML-491 (2 mg/kg). Iproniazid or UML-491 alone had no significant effect on behavior, while phentolamine produced slight depression and reserpine produced a catatonic state. These results suggest that the paradoxical excitation produced by reserpine is due to catecholamines and not to 5-HT.

Clinica Medica Generale
Università di Firenze
Florence, Italy

1612 Fadiga, E., Gessi, T. & Segata, L. Modificazioni delle risposte del lembo corticocerebellare per effetto di farmaci provvisti di azione sinaptica. [Changes in the response of the corticocerebellar tract under the influence of drugs with

synaptic action.] Bollettino della Società Italiana di Biologia Sperimentale, 1962, 38, 440-442.

Studies of the response to electrical stimulation in the isolated cerebellar cortex of the cat following administration of various drugs (either applied directly to the cortex or injected i.a.) showed that only acetylcholine had the theoretically expected effect of a chemical mediator of nerve transmission (initial excitation followed by depression), making it unlikely that histamine (producing general excitation) or ATP (not producing any significant changes) play this role. The general excitation produced by strychnine and tubocurarine and the depressant effect of GABA confirm the hypothesis that they block the inhibitory synapses of the cortex.

Istituto di Fisiologia Umana
Università di Bologna
Bologna, Italy

1613 Heine, W., & Kirchmair, H. Tierexperimentell Untersuchungen zur Frage der teratogenetischen Wirkung des Contergans. [Animal tests of the teratogenic effects of thalidomide (Contergan).] Wochenschrift für die gesamte Medizin, 1962, 17, 1429-1431.

Thalidomide was administered to 3 groups of 12 gravid female rats at dosage levels of 2, 4, and 8 mg/kg/day, beginning 1-3 days after fertilization. The animals were killed on the 20th day and the fetus removed and examined. At 2mg/kg, 7 were gravid, with nearly normal numbers of fetuses, one uterus showing a number of placental fragments without fetuses. In the middle group, 4 were gravid and 3 bled from the vagina during the latter days of pregnancy. Of these, 1 had no fetuses. In the third group 5 were gravid, and of these 3 had placental fragments without fetuses. Among the living fetuses, particularly at 8 mg/kg, there was a marked tendency to dwarfism, and in some cases there was hydrocephalus.

Universitäts Kinderklinik
Rostock, Germany

1614 Böhmer, Dieter & Rügheimer, Erich. Die Folgen der intraarteriellen Injektion von Barbituraten und deren Therapie. [Consequences of intra-arterial injection of barbiturates and their treatment.] Anaesthesist, 1962, 11, 112-113.

Hexobarbital and thiopental (50-350 mg) were injected into the femoral artery of 60 dogs in the form of 2.5, 5.0 and 10% solutions. Higher dosages were always fatal. Depending on the dosage, the effects varied from mild perivascular edema and muscular discoloration to swelling of the walls of the small arteries, vacuolar degeneration and necrosis. Hexobarbital was less toxic. In 2.5% solution, 300 mg of thiopental led only to slight discoloration, but at 5% there was vacuolar degeneration, well-defined edema, a washed-out appearance of the tissues, and swelling of the small arteries. A 10% solution intensified the damage. Spasms of the blood vessels occurred in all animals with both drugs, lasting for 4 minutes, but were not the cause of the later damage. The effects of intraarterial injection can be treated with hydergin, methylprednisolone, calcium and vitamin C. Some ways of avoiding intraarterial injections are suggested.

Chirurgische Universitäts Klinik
Erlangen, Germany

1615 Bräunlich, H., & Hofmann, H. Pharmakologische Studien über N-Allylnormorphinan. [Pharmacological studies on N-allylnormorphinan.] Arzneimittel-Forschung, 1962, 12, 174-178.

Measurements of respiration and blood pressure in rats showed that the effects of lethal doses of morphine (50 mg/kg) and codeine (150 mg/kg) could be counteracted by either prophylactic or subsequent administration of N-allylnormorphinan (1 mg/kg). With both drugs, respiration either reached or approached normality after repeated therapeutic doses, but the hypotensive effects of morphine could not be fully overcome. Prophylactic

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treatment was less effective and generally merely modified the response. The shorter the interval between morphine and N-allylnormorphinan injections, the more clearly were the depressant effects of the former expressed. The effects of codeine were generally more readily counteracted, but the antagonist was unable to overcome respiratory depression due to codeine if the respiratory volume was permitted to fall to values as low as 30% of the initial. At 1 mg/kg, N-allylnormorphinan also counteracted the analgesic effect of morphine (15 mg/kg) in mice. When

administered by itself, however, the antagonist had an analgesic effect at doses of 50-100 mg/kg and showed depressive effects on respiration and blood pressure similar to those of morphine and codeine.

Institut für Pharmakologie
Friedrich Schiller Universität
Jena, Germany

See also 1381, 1523, 1639, 1640, 1646, 1616, 1627, 1630.

1616 Protiva, M., Rajsner, M., Seidlová, V., Adlerová, E., & Vejdelek, Z.J. Derivate des 6, 11-dihydrodibenz (b,e) thiepins, eine neue Gruppe von psychotropen Substanzen. [Derivatives of 6, 11-dihydrodibenz (b,e) thiepins, a new group of psychoactive substances.] *Experientia*, 1962, 7, 326-328.

The chemical synthesis of a number of heterocyclic compounds from phthalide, 6-chlorophthalide and thiophenol is described and the melting points of the resulting derivatives are listed. Preliminary experiments showed that some of these compounds, particularly prothiaden, have ataractic activity in animals (rotating rod test, potentiation of thiopental narcosis) and an imipramine-like effect in man.

Research Institute for Pharmacy and Biochemistry
Prague, Czechoslovakia

1617 Milthers, Kirsten. The N-demethylation of morphine in rats. Quantitative determination of normorphine and morphine in the urine and faeces of rats given subcutaneous morphine. *Acta Pharmacologica et Toxicologica*, 1962, 19, 149-155.

Urinary and fecal excretion of normorphine and morphine was studied in male rats after s.c. treatment with morphine in increasing doses (10-50 mg/kg). A modification of the method of Milthers was used for the analyses. Morphine recovery was 40-50% in the urine and 7-10% in the feces; relative urinary excretion increased with increasing doses of morphine. Six or 7% normorphine was found in urine and 2-3% in feces, independently of the dose of morphine. It was concluded that 12-13% of the morphine administered was transformed to normorphine in rats.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

1618 Svendsen, A. Baerheim., & Brochmann-Hanssen, E. Gas chromatography of barbiturates. II. Application to the study of their metabolism and

excretion in humans. *Journal of Pharmaceutical Sciences*, 1962, 51, 494-495.

A single p.o. dose of barbiturate (200 mg metharbital, 300 mg barbital, 200 mg phenobarbital, 150 mg mephobarbital and 150 aprobarbital) was administered to normal humans. Urine samples were collected at intervals from 9 to 48 hours after drug ingestion and analyzed by gas chromatography for unchanged compounds and metabolites. The demethylation of N-methyl substituted barbiturates could be followed, p-hydroxy phenobarbital was detected after ingestion of phenobarbital and mephobarbital. Only barbital was quantitatively excreted unchanged (for a period of up to 16 days).

School of Pharmacy
University of California
Medical Center
San Francisco, Calif.

1619 Kato, R., Chiesara, E., & Vassanelli. The in vitro inhibition of pentobarbital metabolism by chlorpromazine. *Experientia*, 1962, 18, 269-270.

Metabolized pentobarbital in liver slices from male Sprague-Dawley rats was estimated manometrically. The addition of 2×10^{-4} M chlorpromazine inhibited pentobarbital metabolism by 44% and 8×10^{-4} M chlorpromazine inhibited this activity by 81%. The inhibition of pentobarbital metabolism by chlorpromazine may not be due to a competitive requirement for TPNH, because the addition of TPN, glucose-6-phosphate and nicotinamide did not reverse the inhibition.

Istituto di Farmacologia e di Terapia
Università di Milano
Milan, Italy

1620 Garrett, Edward R. Characterization and mode of degradation of the neurophysiologically important transaminase inhibitors, the α -aminooxyalkanoic acids. *Journal of Pharmaceutical Sciences*, 1962, 51, 572-576.

The titrimetric characterization, stability

and possible modes of degradation of 2 representative compounds, aminooxyacetic acid and β -aminooxypropionic acid, were studied in order to obtain data to elucidate the differences observed in in vivo activity. The former compound showed good inhibition of enzymatic transamination of GABA- α -ketoglutaric acid to glutamate-succinyl-semialdehyde; the latter acid was of low potency in this respect. The biological activity of aminooxyacetic acid may be due to the absence of basicity of the aminooxy group in aqueous solution perhaps due to a tendency to form a 5-membered ring, thus imparting to the molecule the ability to cross cellular membranes more readily. These α -aminooxyalkanoic acids may carry and release hydroxylamine (a transaminase inhibitor) at the physiological site, while hydroxylamine itself may not be readily transportable or metabolized. It is even possible that the intact acids may act as primary agents.

Research Division
Upjohn Company
Kalamazoo, Mich.

1621 Portmann, Glenn A., & Harris, Loyd E. Barbiturate glucosides. *Journal of Pharmaceutical Sciences*, 1962, 51, 780-782.

Nitrogen glucosides of barbital, phenobarbital, amobarbital, secobarbital and pentothal were prepared. Proof of the nitrogen glucosidic linkage was obtained by direct condensation of sym-di-(tetra-O-acetyl- β -D-glucopyranosyl)-urea with diethylmalonyldichloride. The syntheses and chemistry of these new compounds are described in some detail. A comparison is made between the barbiturates (40-200 mg/kg) and their glucosides (500-2000 mg/kg) for hypnotic activity in rats. Both the enolic tetraacetate and nitrogen type glucosides were inactive, even at 6-25 times the hypnotic dose of the corresponding barbiturate salt. No biological details were presented.

Research Department
White Laboratories, Inc.
Kenilworth, N. J.

1622 Ganrot, P.O., Rosengren, E., & Gottfries, C.G. Effect of iproniazid on monoamines and monoamine oxidase in human brain. *Experientia*, 1962, 18, 260-261.

Sixteen terminal cancer patients were investigated at autopsy; 5 received iproniazid and 11 served as controls. Bodies were sent to the mortuary within 2 hours after death and autopsied within 3-70 hours. Slices were taken from the parietal region of the cortex, head of the caudate nucleus unilaterally, the mesencephalon and the liver for estimations of MAO activity. The mean MAO activity found in the cortex according to the manometric method of Creasey (1956) in the 11 controls was 9 μ M/g/hour. Activity in the caudate nucleus and mesencephalon was about 16 μ M/g/hour; somewhat greater variation was observed in liver MAO activity, 50-100 μ M/g/hour with a mean of 68 μ M/g/hour. In the 5 cases treated with iproniazid the values found were much lower than those observed in controls, thus in 3 cases treated 1-3 weeks before death with 75-125 mg daily, the MAO activity was less than 5% of the mean control value, with an increase in cerebral catecholamines and 5HT. Conventional iproniazid treatment has an inhibitory effect on brain and liver MAO activity and increases the concentration of monoamines.

Department of Pharmacology
University of Lund
Lund, Sweden

1623 Popelak, A., & Lettenbauer, G. *Rauwolfia Alkaloide IX. Über die Verätherung der Yohimban-Alkaloide mit Diazomethan.* [Rauwolfia alkaloids IX. Synthesis of the ethers of yohimbane alkaloids using diazomethane. *Archiv der Pharmazie*, 1962, 295, 427-430.

The methylation of alcoholic hydroxyl groups is discussed and chemical and chromatographic experiments with derivatives of yohimbine, α -yohimbine, methylreserpate and methyl deserpidate are reported briefly. Synthetic techniques

and R_f values are given.

Forschungslaboratorium
Firma C.F. Boehringer u. Söhne G.m.b.H.
Mannheim-Waldhof, Germany

1624 Syner, Frank N., & Shaw, Charles R.
Effect of schizophrenic serum on in vitro
synthesis of glutamine and gamma-amino-
butyric acid. *Comprehensive Psychiatry*,
1962, 3, 309-313.

A comparative study was carried out on the
effects of serum from 10 adult schizo-
phrenic males, 9 adult males with person-
ality disorders, 9 male schizophrenic child-
ren and 8 male children with other disorders
on the in vitro synthesis of glutamine and
GABA by rat brain acetone powder, using
glutamate as the substrate. Glutamine
production was markedly decreased by add-
ition of either schizophrenic or control
serum, while GABA formation was un-
affected by both. Thus, if there is an ab-
normal substance in schizophrenic serum,
it does not interfere directly with glutamine
or GABA synthesis. The selective inhibition
of glutamine synthesis by normal serum is
still unexplained.

Hawthorn Center
Northville, Mich.

1625 Amemori, T. Effect of dibenzyline
on serum cholesterol in rabbits. *Exper-
ientia*, 1962, 18, 331-332.

Levarterenol bitartrate was given i.m.,
0.6 mg once a day for 2 days to 26 rabbits.
Twenty mg of 5HT were given i.m. to 12
animals as an aqueous solution of 5HT
creatinine sulfate once a day for 2 days.
Dibenzyline in doses of 2.5 mg/kg was
injected into the ear vein of 17 animals
over a 20 minute period (1 rabbit died
and another showed serious symptoms of
adrenergic blockade, later recovering).
Blood was taken before and 24 hours after
injection and serum cholesterol was
eliminated. Cholesterol decreased slightly
(mean 3.6%) after the administration of
levarterenol and the cholesterol change due
to serotonin treatment was insignificant.
However, 24 hours after single i.v.

injections of dibenzyline the cholesterol
level increased significantly (mean 13.5%).

Department of Anatomy
University of Saskatchewan
Saskatoon, Saskatchewan
Canada

1626 McDonald, Roger K., & Weise,
Virginia K. The effect of certain psycho-
tropic drugs on the urinary excretion of
3-methoxy-4-hydroxy-mandelic acid in man.
*Journal of Pharmacology and Experimental
Therapeutics*, 1962, 136, 26-30.

The effect of single doses of reserpine
(2.5 mg i.m.), chlorpromazine (200 mg
p.o.), meprobamate (800 mg p.o.),
morphine sulfate (16 mg i.m.), pentobarbital
(200 mg p.o.) and d-amphetamine sulfate
(15 mg p.o.) on the urinary excretion of
3-methoxy-4-hydroxymandelic acid and
creatinine during the 24 hours following drug
administration was investigated in a placebo-
controlled study on 16 normal human subjects.
Only reserpine, morphine and chlorpromazine
had a significant effect. Whereas reserpine
increased 3-methoxy-4-hydroxymandelic
acid excretion and decreased that of
creatinine, morphine decreased both
significantly so that the ratio of the 2
compounds remained relatively constant,
and chlorpromazine decreased 3-methoxy-
4-hydroxymandelic acid excretion while that
of creatinine was unchanged. The increased
excretion of 3-methoxy-4-hydroxymandelic
acid following reserpine is thought to be
due to depletion of tissue catecholamines and
not to increased renal clearance; similarly,
the decrease following chlorpromazine can be
attributed to a direct effect on catecholamine
metabolism. The effect of morphine, how-
ever, was accompanied by a decrease in
urine volume and is attributed, at least in
part, to effects on renal function. Studies
of tryptamine excretion indicated that
amphetamine also had no significant effect
on MAO activity in these experiments.

Laboratory of Clinical Science
National Institute of Mental Health
NIH
Bethesda, Md.

- 1627 Doepfner, W. Biochemical observations on LSD-25 and Deseril. *Experientia*, 1962, 18, 256-257.

Extraction and fluorimetric estimation of LSD and methysergide (Deseril) were carried out on the brains of female rats 20 minutes after i. v. injection of the following doses of LSD: 1, 3 and 10 mg/kg and methysergide: 1, 3, 10 and 30 mg/kg. Almost instantaneously after the injection of LSD, as low as 1 mg/kg, the animals showed hyperactivity with convulsive movements and at higher doses generalized body tremors. After methysergide no behavioral changes were observed except slight hypersensitivity to noise and handling. Additionally lung, muscle and blood were assayed. The levels of LSD compounds in blood and muscle are about the same but definitely lower than those in the lungs. In the case of LSD the brain values closely resembled those found in muscle and blood, but much lower levels of methysergide were detected in this tissue. This difference in brain concentration is probably due to differential penetration across the blood-brain barrier. Only about 13% of methysergide reaches the brain.

Medizinisch-Biologische Forschungsabteilung
der Sandoz A.G.
Basel, Switzerland

- 1628 Goldstein, M., & Contrera, J.F. The effect of pH on enzymatic formation and inhibition of norepinephrine synthesis. *Experientia*, 1962, 18, 332-333.

The effect of pH on the conversion rate of dopamine to levarterenol (norepinephrine) and epinine to epinephrine by phenolamine- β -hydroxylase was studied and the pH effect on the inhibition of the dopamine to levarterenol conversion by various inhibitors was examined. Maximal enzymic activity was established at pH 5.5. The formation of levarterenol and epinephrine was diminished in an incubation mixture with phosphate buffer compared to an incubation mixture containing acetate buffer; EDTA also inhibited levarterenol formation. The effects of pH may be due to ionization of enzymatically active sites or cofactors and may also affect the stability of the substrate-

enzyme or intermediate product-enzyme complex. The inhibition of levarterenol synthesis by DOPA, tryptamine and adrenalone was measured and DOPA and tryptamine inhibition were optimal at pH 5.5, while adrenalone inhibition had its optimum at pH 6.4.

Neurochemistry Laboratory
Department of Psychiatry and Neurology
New York University School of Medicine
New York, N. Y.

- 1629 Barondes, Samuel H. The influence of neuroamines on the oxidation of glucose by the anterior pituitary. I. The role of monoamine oxidase. *Journal of Biological Chemistry*, 1962, 237, 204-207.

The bitartrate salts of L-epinephrine and L-levarterenol and the creatinine sulfate complex of serotonin were assayed for effects on glucose oxidation using beef anterior pituitary slices. Radioactive glucose, (75 mg/100 ml; 500,000 cpm per flask) was used and results measured with a liquid scintillometer. Other amines were also used, including an aliphatic amine and shared with epinephrine, levarterenol and serotonin, the ability to stimulate glucose oxidation. α -Methylated amines which are not substrates of monoamine oxidase do not share this property and the stimulation induced by the active amines can be blocked by monoamine oxidase inhibitors, i. e., pheniprazin and Al 9120. A number of aldehydes also stimulated glucose oxidation which was not blocked by MAO inhibitors. Related acids and alcohols were inactive. A possible "nondegradative" role of MAO is considered.

Clinical Endocrinology Branch
National Institute of Arthritis and Metabolic Diseases
NIH
Bethesda 14, Md.

- 1630 Johnsen, U. E., Jacobson, C. R., LaForge, R. A., & Hanna, Calvin. Preparation and pharmacological properties of some benzyl derivatives of diphenylacetic acid. *Journal of Pharmaceutical Sciences*, 1962, 51, 799-801.

Various benzyl derivatives of diphenylacetic acid were synthesized; their syntheses and chemistry are summarized. Lack of aqueous solubility limited pharmacologic testing. No toxicity was noted at 1.0 g/kg p.o., but antispasmodic activity similar in potency to that elicited by atropine was indicated for N-benzyl-N-methyl-2-chloro- and the N-benzyl-2-hydroxy-diphenylacetamides, as they inhibited the passage of a charcoal meal. No cardiovascular or respiratory effects were noted i.v. N-benzyl-2-hydroxy and N-benzyl-2-acetoxy diphenylacetamides (40 mg/kg) showed antipentamethylene tetrazol (100 mg/kg s.c.) activity i.p.; the former (at 100 mg/kg) also abolished the convulsive actions of electric shock. No sedative or tranquilizer activity was noted in the "wild" hamster (hungry or incited to anger) at 40 mg/kg.

Research Laboratory of Bilhuber-Knoll Corp.
Orange, N. J.

1631 Yard, Allen S., & McKennis, Herbert, Jr. Aspects of the metabolism of isoniazid and acetylisoniazid in the human and the dog. *Journal of Medicinal and Pharmaceutical Chemistry*, 1962, 5, 196-203.

The metabolism of isoniazid (100-150 mg/kg i.v. in dogs) and acetylisoniazid (265 mg i.v. in dogs and 500 mg p.o. in normal males) was studied in normal males and dogs. The urine was analyzed for drug metabolites, using extraction procedures, chromatography and ion exchange techniques. Administration of 1-acetyl-2-isoniazid yielded 1,2-diacetylhydrazine in human urine and acetylhydrazine in dog urine. Since the dog could not form 1,2-diacetylhydrazine from hydrazine or acetylhydrazine, it was concluded that the metabolism of isoniazid in man and certain other species (i.e., rabbit) involves the following route:
isoniazid $\longrightarrow$ 1-acetyl-2-isoniazid $\longrightarrow$ acetylhydrazine $\longrightarrow$ 1,2-diacetylhydrazine.

Department of Pharmacology
Medical College of Virginia
Richmond, Va.

1632 Ullmann, Elsa & Kassalitzky, Horst. Nachweis und Bestimmung von Reserpin in

Anwesenheit von Lösungsvermittlern.
[Identification and determination of reserpine in the presence of surface-active agents.] *Archiv der Pharmazie*, 1962, 295, 37-40.

The ways in which solubilizing agents interfere with the classical analytical techniques for reserpine and rescinnamine are reviewed and experiments on the chromatographic separation of these alkaloids from Tween-20 on formamide-treated silica-gel plates are reported. The solvent system consisted of n-heptane and methylethylketone. After separation, reserpine was determined spectrophotometrically.

Institut für Pharmazie und Lebensmittelchemie
Universität München
Munich, Germany

1633 Balzer, H., & Palm, D. Über den Mechanismus der Wirkung des Reserpins auf den Glykogengehalt der Organe. [Mechanism of the effect of reserpine on the glycogen level in organs.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 65-84.

Administration of reserpine (5 mg/kg s.c.) to female mice increased the glycogen content of the brain, liver, heart and skeletal muscle, the increase being due entirely to free (trichloroacetic acid extractable) glycogen. Epinephrine (500 μ g/kg i.m.) and levarterenol (500 μ g/kg i.m.) produced transitory decreases in liver and muscle glycogen, but had no effect on the cerebral glycogen level. ACTH and hydrocortisone increased liver and muscle glycogen appreciably, but had little effect in the brain. Experiments with C^{14} -alanine showed that reserpine increased gluconeogenesis and glycogen turnover, with increased specific activity in both free and bound fractions. Experiments with C^{14} - γ -aminoisobutyric acid showed that reserpine increased the influx of amino acids into the liver but decreased their influx into the brain. Iproniazid (100 mg/kg i.m.), however, increased this influx into the brain.

Pharmakologisches Institut
Universität Frankfurt a. M.
Frankfurt, Germany

1634 Gunne, Lars-M. Catecholamine metabolism in morphine withdrawal in the dog. *Nature*, 1962, 195, 815-816.

Increasing doses of morphine (3-100 mg/kg/day) were administered to 10 dogs for 2 months, and 24 hours after 5 of the dogs served as controls and 5 received 2 doses of nalorphine (10 mg/kg) at 2 hour intervals animals were sacrificed, and their brains analyzed for catecholamine content. Previously collected urine eluates and adrenals were also analyzed for catecholamines. Nalorphine increased epinephrine excretion markedly. Morphine at minimal doses increased urinary excretion of epinephrine and levarterenol initially, but levels returned to the normal range within 10 days. After animals were sensitized to morphine (90 mg/kg/day), 1 injection of nalorphine resulted in a marked increase in epinephrine for 1 day, with a persistent concomitant increase of urinary levarterenol which continued for several days. Withdrawal of morphine was accompanied by a sharp rise in epinephrine excretion followed by a moderate increase in levarterenol. Morphine sensitized animals with nalorphine induced abstinence showed a significant decrease in brain and organ catecholamine content, and a particularly pronounced decrease was observed in animals which exhibited the severest abstinence symptoms.

Department of Physiology
Karolinska Institute
Stockholm, 60, Sweden

1635 Put, T.R., & Hogenhuis, L.A.H. Brain serotonin and thyroid function. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 10, 343-352.

Determinations of the cerebral 5HT levels at autopsy in rats treated for 2 weeks with either thyroxine (25 or 50 μ g/100 g/day s.c.) on propylthiouracil (0.075% solution ad libitum) showed that both agents produced hypothyroidism and a significant increase in cerebral 5HT. Thyroidectomy, however, did not increase the cerebral 5HT level. Rats treated with propylthiouracil also showed adrenal hypertrophy, probably secondary to the increased blood levels of 5HT.

Michael Reese Hospital
Chicago, Ill.

1636 Milthers, Kirsten. N-Dealkylation of morphine and nalorphine in the brain of living rats. *Nature*, 1962, 195, 607.

Anesthetized male rats were eviscerated, after which morphine or nalorphine (100 mg/kg i.v.) was injected. Decapitation ensued after 15 minutes, and blood samplings from the wound plus brain tissue were analyzed for normorphine, morphine and nalorphine. Brain tissue was also analyzed from rats given morphine (26 μ g/g and normorphine (1.2 μ g/g). While 5% of the total morphine content was found as normorphine in the brain, only 1% of blood morphine was normorphine. In 4 rats given nalorphine brain concentrations were nalorphine, 257 μ g/g and normorphine, 4.6 μ g/g. Morphine and nalorphine were transformed into normorphine in rat brain tissue in vivo.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

1637 Benedict, R.G., Brady, L.R., & Tyler, V.E. Jr. Occurrence of psilocin in *Psilocybe baeocystis*. *Journal of Pharmaceutical Sciences*, 1962, 51, 393-394.

The isolation and characterization of psilocin is reported from the mushroom *Psilocybe baeocystis*, found in the north-western U.S. Chromatography was utilized to identify the extracted material and a substance having referents similar to those of psilocin was located. Though psilocybin could not be detected, psychotropic activity followed its ingestion and the plant may thus be considered hallucinogenic (the 2nd such species in its geographical area).

College of Pharmacy
University of Washington
Seattle 5, Wash.

1638 Brochmann-Hanssen, E., & Svendsen, A. Baerheim. Gas chromatography of sympathomimetic amines. *Journal of*

Pharmaceutical Sciences, 1962, 51, 393.

This brief communication reports the separation and identification of micro-quantities of sympathomimetic amines by gas-liquid chromatography, at temperatures ranging from 104° for nonphenolic to 135° for phenolic amines. A typical sample constituted 1.0 µl of a solution containing 0.5-1.0% of each amine. The substances mentioned include amphetamine, methamphetamine, mephentermine, phenylpropanolamine, epinephrine and pseudoepinephrine.

School of Pharmacy
University of California
San Francisco 22, Calif.

1639 Kato, Laszlo, Gozsy, Bela., Lehmann, H. E., & Ban, T. A. Attempt to classify psychotropic drugs, based on their affinity to mucopolysaccharides in vivo. Journal of Clinical and Experimental Psychopathology and Quarterly Review of Psychiatry and Neurology, 1962, 23, 75-90.

An attempt was made to classify many different psychotropic drugs, used at various dosages, based on their in vivo i.v. effect in Sprague-Dawley rats on the dextran (0.7-25 mg/0.5 ml) reactive sites, one responsible for formation of edema and the other for its inhibition. The drugs were dissolved and diluted in dextran solutions, then administered i.v. Evaluation was based on a standard dose, the amount of dextran evoking 100% intensity within 15 minutes in rats; the critical dose, the amount that did not quite provoke increased capillary permeability and visible edema; and the degree (in percentage) of edema compared to the maximum possible. Drugs with established antipsychotic properties reacted with both reactive sites of dextran. CNS stimulants and antidepressants, except MAO inhibitors, reacted exclusively with the edema-inhibiting site. An attempt was made to correlate these effects with clinical behavioral effects. The method is proposed as valuable for rapid drug screening.

Institute of Microbiology and Hygiene
University of Montreal
Montreal, Quebec
Canada

1640 Fikrat, Hikmat T., & Oneto, J. F. Derivatives of thiazolo[5,4-d]thiazole. Journal of Pharmaceutical Sciences, 1962, 51, 527-529.

The chemistry, synthesis and biological activity of a series of bis-2,5-substituted thiazolo [5,4-d] thiazoles was described in full. Rat blood cholesterol levels were increased 20% by oral administration of bis-(4-aminophenyl)-thiazolothiazole (5 mg/day) for 7 days. The 1,1-dimethyl-3-cyanopropyl derivative induced normal sleep in various animals at 2-200 mg/kg, had an acute mouse LD50 of 1250 mg/kg s.c., intensified the effect of pentobarbital at 25-200 mg/kg i.p., showed only minor protection against pentylenetetrazol convulsions, had no autonomic or cardiovascular effects in anesthetized dogs at 50 mg/kg (a dose tolerated by unanesthetized dogs) and no analgesic effect, strychnine antagonism or protection against apomorphine emesis. Unlike the tranquilizers, it neither altered autonomic function nor exhibited central stimulation.

School of Pharmacy
University of California Medical Center
San Francisco 22, Calif.

1641 Shapiro, Seymour L., Bazga, Theodore, & Freedman, Louis, Indanols, V. Indanoxyacetic acid derivatives. Journal of Pharmaceutical Sciences, 1962, 51, 582-584.

A number of indanoxyacetic acid derivatives were prepared, their chemical properties were tabulated and their syntheses summarized. The hypocholesteremic effect of α-(indan-4-oxy) butyric acid was observed. Other compounds from this group showed adrenergic blocking and potentiating effects, tranquilizing activity and antiinflammatory action. No methodological details were given for bioassay procedures.

Research Laboratories
U.S. Vitamin and Pharmaceutical Corp.
26 Vark Street
Yonkers 1, N. Y.

1642 Schieser, David W., & Tuck, Dallas L. Free radical studies by electron-spin resonance of some derivatives of phenothiazine. *Journal of Pharmaceutical Sciences*, 1962, 51, 694-695.

Prochlorperazine, chlorpromazine, trifluorpromazine and perphenazine were oxidized so that electron-spin resonance spectra of their free radicals could be determined. This technique demonstrated the existence of stable free-radical semiquinoid intermediates in the oxidation of these compounds. The spectra of the intermediates differed from those of the parent compounds in the lack of hyperfine structures. Relevant chemical details were presented briefly.

School of Pharmacy
University of California
San Francisco 22, Calif.

1643 Lange, Winthrop E., Candon, Basil H., & Chessin, Max. Metal chelates of oxazolidinones as central nervous system stimulants. *Journal of Pharmaceutical Sciences*, 1962, 51, 477-480.

A series of metal chelates was prepared of 2-imino-5-phenyl-4-oxazolidinone (pemoline), 2-imino-5,5-diphenyl-4-oxazolidinone and 2-imino-5-p-biphenyl-4-oxazolidinone, using cupric, nickel, magnesium and ferric ions. Their chemistry is described. The effects of chelation upon CNS stimulating activity were studied in mice. The compounds were usually tested at 100-500 mg/kg p.o. The magnesium chelate of pemoline exhibited the selective CNS stimulating characteristics of the parent compound, as well as an earlier onset of action and a relatively shorter span of activity. Substitution at position 5 inhibited the activity of these compounds.

Massachusetts College of Pharmacy
Boston, Mass.

1644 Nitze, H.R., & Remmer, H. Der Einfluss von Barbituraten auf die Förderung der Glucuronsäureausscheidung. [The effect of barbiturates on the stimulation of glucuronic acid excretion.] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 242, 555-563.

Administration of various barbiturates (80-200 mg/kg/day s.c.) to rats produced a significant increase in urinary excretion of glucuronic acid, but had no effect on glucuronide excretion, following administration of salicylamide or sodium salicylate. Glucuronide and glucuronic acid excretion was not affected by diethylaminoethylphenyl diallylacetate, which inhibits microsomal oxidative enzymes, so that stimulation of glucuronic acid excretion by barbiturates is a more unspecific process.

Pharmakologisches Institut
Freie Universität Berlin
Berlin, Germany

1645 Johannesson, Torkell. Morphine as an inhibitor of brain cholinesterases in morphine-tolerant and non-tolerant rats. *Acta Pharmacologica et Toxicologica*, 1962, 19, 23-25.

Large doses (600-780 mg/kg i.p.) of morphine were given to morphine-tolerant and nontolerant male rats. The nontolerant rats died 20-60 minutes after drug injection; tolerant rats were sacrificed at the same time. The cerebral morphine contents from both groups of rats was 20-40 $\mu\text{g/g}$, as determined by the polarographic method of Milthers. Brain cholinesterase activity was determined with and without added morphine by the method of Jensen-Holm et al. Using acetylcholine iodide (6.3×10^{-6} M) as the substrate, cholinesterase activity was found to be the same in both groups of rats; this activity was reduced 30-60% in either group by morphine. CNS cholinesterase inhibition following large doses of morphine was postulated as the cause of the excitation in both tolerant and nontolerant rats.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

Institut für Pharmazie und Lebensmittel-
chemie
Universität München
Munich, Germany

1646 Ebert, Andrew Gabriel. Barbitol
 C^{14} distribution and metabolism in
tolerant and non-tolerant rats. Ann
Arbor: University Microfilms Inc. No.
62-3447. Pp. 61.

Barbital tolerance was induced in male
Holtzman rats over a 2-week period through
administration of increasing i. p. doses.
Seventy-two hours after the last pretreat-
ment dose, control and pretreated animals
were given 200 mg/kg barbital i. p. Lag
times between the 2 groups did not differ
but sleep times were 13-56% shorter in
the pretreated animals. Barbitol C^{14}
was administered i. v. to tolerant and non-
tolerant groups. At 10-360 minutes after
drug administration the animals were
sacrificed. Brain, plasma and urine
samples were assayed for radioactivity.
No difference in brain, plasma or urine
barbital levels was observed between
tolerant and nontolerant rats, which
indicates that barbital tolerance cannot
be ascribed to decreased blood-brain
barrier permeability, decreased drug
absorption or increased drug excretion
in the tolerant animal. Monoethyl
barbituric acid and barbital were identified
chromatographically in the urine.

The Squibb Institute for Medical Research
New Brunswick, N. J.

1647 Thies, H., & Özbilici, Z. Die
spektralen Eigenschaften der Sympatho-
mimetica und Weckamine. [The spectral
properties of sympathomimetics and
amphetamines.] Archiv der Pharmazie,
1962, 295, 194-196.

Typical UV-absorption spectra for
representatives of the phenylalkyl- and
phenylalkanolamines, p-hydroxyphenylalkyl-
amines, p-hydroxyphenylalkanolamines,
m-hydroxyphenylalkanolamines, 3,4-
dihydroxyphenylalkanolamines and diphenol-
keto-bases are shown and described. The
spectral properties were found to be
correlated with chemical structure.

1648 Machata, G. & Kisser, W. Nach-
weis von Hydantoinderivaten in der
gerichtschemischen Praxis. [Determi-
nation of hydantoin derivatives in toxicologi-
cal practice.] Archiv für Toxikologie,
1962, 19, 327-338.

Since barbiturates and hydantoin derivatives
are usually prescribed together and
cannot be determined quantitatively in
tissue fluids and organs without previous
isolation, techniques for their separation
by sublimation or film chromatography
are discussed. Melting point data,
crystal forms, R_f values and ultraviolet
or infrared absorption spectra are
presented for the principal compounds, the
latter being most useful in the final
determination of relatively pure samples.
Finally, analytical data are presented
on tissue specimens from 4 fatal cases
of drug intoxication.

Institut für gerichtliche Medizin
Universität Wien
Vienna, Austria

1649 Lindfors, Raimo & Ruohonen, Aira.
Gerichtstoxikologische Identifizierung
von Bromisoval, Karbromal und ihren
Entbromungsprodukten unter Verwendung
von Infrarotspektroskopie und Dünnschich-
tchromatographie. [Toxicological
identification of bromisoval, carbromal
and their debrominated derivatives using
infrared spectroscopy and film chromato-
graphy.] Archiv für Toxikologie, 1962,
19, 402-407.

R_f values for the chromatographic separa-
tion of bromisoval, 3-methylbutyrylcar-
bamide, carbromal, 2-ethylbutyrylcarbamide
and meprobamate are given and the isola-
tion of these compounds from tissue
samples, urine and specimens of gastric
contents is discussed. Infrared spectro-
scopy is recommended for the final
quantitative determination. Finally,
analytical experience with 23 fatal cases

of bromisoval and/or carbromal intoxication is reviewed briefly and the analytical procedures carried out in 2 cases of intoxication due to meprobamate and brominated sedative are presented in detail.

Institute for Legal Medicine
University of Helsinki
Helsinki, Finland

1650 Pittman, J. A., & Brown, R. W.
Antithyroid activity of amphenidone.
Clinical Endocrinology and Metabolism,
1962, 22, 100-102. [Letter]

Two groups of female Sprague-Dawley rats on I_2 enriched diets received amphenidone (0.6-1.0 mg/g intragastrically b.i.d.) for 7 days before sacrifice; 1 group received a low I_2 diet 12 days before amphenidone administration and a $0.2\mu\text{C}$ dose of I^{131} i.p. on the 7th day of drug administration; a 4th group received amphenidone as a dietary constituent (0.6% and 1% by weight) in a low I_2 diet initiated on the day of drug administration. An amphenone [dosage unspecified] (administered s.c., b.i.d.) treated group provided comparison. A dose of 0.6 mg/g was moderately goitrogenic, and 1.0 mg/g was markedly goitrogenic. The last 2 experiments confirmed the goitrogenicity of amphenidone and demonstrated inhibition of the thyroidal 24-hour uptake of I^{131} . All thyroid changes were significant, except in the 1st experiment ($p > 0.1$). Long term studies by other investigators showed that a slight increase in thyroid weight usually occurred. On the basis of the above information, it appears unlikely that clinical dosages currently advocated will be associated with any overt thyroid dysfunction.

Radioisotope Service
Birmingham VA Hospital
Birmingham, Ala.

1651 Zelnicsek, Eman. Urinary excretion of α -keto acids in phenylketonuria. Clinica Chimica Acta, 1962, 7, 592-593.

Urine from 2 brothers aged 6 and 13 years

with phenylketonuria was analyzed to determine α -ketoglutaric, pyruvic and phenylpyruvic acids by means of descending paper chromatography with a butanol-ethanol-ammonia solvent. Controls included 24 hour urine specimens from parents, a normal sibling and 21 healthy children aged 5-10 years. Chromatograms of hydrazones obtained from the urines of phenylketonuric patients exhibited characteristic spots. In comparison with the normal children, phenylketonurics excreted only about half the normal amount of α -ketoglutarate. Values for pyruvate corresponded to the findings in controls. Normal pyruvate and α -ketoglutarate values were obtained in parents and the normal sibling. The decreased elimination of α -ketoglutarate in phenylketonurics suggests that the excess unmetabolizable phenylalanine is transformed to phenylpyruvate by transamination.

Department of Medical Chemistry
J. E. Purkyne University
Brno, Czechoslovakia

1652 VandenHeuvel, W. J. A., Haahti, E. O. A., & Horning, E. C. Gas chromatographic separations of drugs and drug metabolites. Clinical Chemistry, 1962, 8, 351-359.

Barbiturates (nembutal, pentothal, phenobarbital, etc.), antimalarial drugs (chloroquine, primaquine, quinine, etc.), phenothiazines and diphenylamines (promazine, chlorpromazine, imipramine, etc.) and steroids (androsterone, cholestane, etc.) were analyzed and separated by gas chromatography. Numerous drugs and their metabolites may be estimated and identified by utilizing gas chromatographic methods. The most useful techniques involve the use of columns with relatively thin films of thermostable liquid phases coated on inert or inactivated supports used with high-sensitivity detectors. Separation of barbiturates is facilitated by differences in molecular weights which lead to quite different retention times on columns with a nonselective phase. Selective phases give separations which are based primarily on the nature of the functional groups and only secondarily on molecular size. An unknown

compound may be positively identified by using 2 gas chromatographic columns.

Lipid Research Center
Baylor University College of Medicine
Houston, Tex.

1653 Berry, Helen K., Scheel, Carolyn, & Marks, Joy. Microbiological test for leucine, valine, and isoleucine using urine sample dried on filter paper. *Clinical Chemistry*, 1962, 8, 242-245.

A microbiological assay with *Lactobacillus arabinosus* 17-5 was used to detect valine, leucine and isoleucine in urine specimens dried on filter paper obtained from 700 mentally retarded children under 6 years of age with maple sugar disease, Hartnup disease, etc. All 3 amino acids were detected in 3 specimens, 5 were positive for valine, 4 for leucine and 12 for isoleucine. Two of the 3 specimens that gave positive results in the microbiological assay were eluted for paper chromatographic testing, and showed a generalized amino-aciduria including, cystine, tyrosine, phenylalanine, glycine, alanine and glutamine in addition to valine, leucine and isoleucine. The 3rd specimen yielded valine and leucine/isoleucine upon chromatographic examination. The microbiological test is preferable to chromatographic evaluation to detect valine, leucine or isoleucine in the urine since it involves simple laboratory procedures and is an inexpensive and effective means of screening young children for metabolic disorders such as maple sugar disease.

Children's Hospital Research
Foundation
Cincinnati 29, Ohio

1654 Ernsting, M.J.E., Kafoe, W.F., Nauta, W.Th., Oosterhuis, H.K., & Roukema, P.A. Investigation into the effect of orphenadrine hydrochloride (Disipal) on the monoamine oxidase in the brain and liver of rats and guinea pigs. *Medicina Experimentalis*, 1962, 7, 119-124.

Orphenadrine (60 mg/kg) was administered orally to rats 1 hour prior to sacrifice,

after which MAO activity was determined in the brain and liver tissue. The serotonin content of rat brain was determined spectrofluorometrically 1 and 2 hours after oral administration of orphenadrine (100 mg/kg) and 1 hour after an injection of reserpine (1 mg/kg i.v.) preceded by oral administration of orphenadrine (100 mg/kg) 1 hour previously. In vitro experiments with orphenadrine (2.5×10^{-3} M - 5×10^{-4} M) and diphenhydramine (5×10^{-4} M) as inhibitors and tyramine (0.01 M) as substrate were performed on rat brain and liver homogenates with and without KCN. With orphenadrine (5×10^{-4} M), harmine (5×10^{-4} M - 1.4×10^{-6} M) and iproniazid (5×10^{-4} M) as inhibitors and tyramine (0.01 M) as substrate, MAO inhibition was determined in guinea pig brain and liver mitochondrial preparations. With 5HT (0.001 M) as substrate, and orphenadrine (5×10^{-4} M) and harmine (5×10^{-4} M) as inhibitors, MAO inhibition was determined in a mitochondrial suspension of rat liver and brain tissue. With respect to in vitro testing, Hope and Smith's method yields 60% MAO inhibition in brain and liver homogenates at a concentration of 2.5×10^{-3} M. KCN inhibits endogenous oxidation, but makes MAO more sensitive to inhibitors. The effect of orphenadrine is comparable to that of diphenhydramine. Orphenadrine shows hardly any effect on MAO with Gey and Pletscher's method, but harmine and iproniazid correspond to values obtained from the literature. Measurement of 5HT consumption revealed that orphenadrine failed to affect MAO. In vivo administration of orphenadrine to rats also failed to affect MAO activity or influence the 5HT content of rat brain. Reserpine-induced depletion of 5HT was not counteracted by orphenadrine.

N. V. Koninklijke Pharmaceutische
Fabrieken
v/h Brocades-Stheeman & Pharmacia
Amsterdam, The Netherlands

1655 Madsen, Ole Drachmann. Colorimetric determination of meprobamate in blood. *Clinica Chimica Acta*, 1962, 7, 481-487.

Ten ml amounts of plasma or serum

(specimen), standard meprobamate solution (10 mg/l) and a water blank are placed in 40 ml tubes. Two drops of ammonium hydroxide, 2 drops of saturated potassium chloride and 25 ml of carbon tetrachloride-chloroform are added. The mixture is then centrifuged and the solvent layer containing meprobamate removed and filtered. A red-violet color is then developed by the addition of 2 ml of a saturated solution of antimony trichloride in glacial acetic acid and 2 ml p-dimethylaminobenzaldehyde reagent. Specimens are then read colorimetrically at 550 m μ . The method has an accuracy of $\pm 5\%$, and is suitable for clinical purposes. It has been used to measure the dosage of meprobamate during the treatment of tetanus, and in the diagnosis of poisoning. The maximum concentration in blood appears 2 hours after administration of meprobamate. Poisoning cases have shown a maximum of 120 mg/l and therapeutic dosage a range of 1-33 mg/l.

Central County Hospital
Department of Clinical Chemistry
Nykoebing F., Denmark

1656 Van Pilsum, John F., & Halberg, Franz. A method for the determination of argininosuccinic acid in human urine. *American Journal of Mental Deficiency*, 1962, 67, 82-89.

A screening method for the determination of argininosuccinic acid (in amounts above approximately 300-500 mg/day) is described which was used on 192 mentally retarded patients, with no cases of argininosuccinic aciduria found. As argininosuccinic acid (anhydride form) reacts with ortho-nitrobenzaldehyde in the presence of alkali, the presumably oxidized argininosuccinic acid derivative is converted to arginine by heating the neutralized solution. Creatinine, which reacts with ortho-nitrobenzaldehyde in the presence of alkali to yield oxalyl methylguanidine, is converted to methylguanidine by heating the neutralized solution. Treatment of the solution containing methylguanidine and arginine with Ba(OH)₂ and ZnSO₄ will remove the arginine and allow the methylguanidine to remain in solution. Any differences in the color intensities as

measured by a modified Sakaguchi Color Reaction between the Ba(OH)₂ and ZnSO₄ treated solution and the untreated solution are taken as the amount of arginine present (either free or produced from the argininosuccinic acid). This simple, yet specific procedure is described for possible large scale investigation of this relatively rare phenomenon in mentally deficient populations.

Department of Pathology
University of Minnesota Medical School
Minneapolis 14, Minn.

1657 Thies, H., & Ermer, E. Verteilungskoeffizienten und Konstitution bei Weckamin und verwandten Arylalkylaminderivaten. [Chemical structure and distribution coefficients for amphetamines and related arylalkylamine derivatives.] *Naturwissenschaften*, 1962, 49, 37.

Studies of the distribution coefficients of 10 arylalkylamines in ether-water showed that the coefficients of the 8 secondary amines were directly proportional to the number of C atoms outside of the aromatic ring, the coefficient being doubled for every additional C atom in the side chain. The distribution coefficient was unaffected by the configuration of the side chain or the position of the amino group, except that the 2 primary amines gave anomalous results.

Institut für Pharmazie und Lebensmittelchemie
Universität München
Munich, Germany

1658 Sanz Gadea, R. Acción de la clorpromacina sobre la vitamina C en orina de rata y cobaya. [Effect of chlorpromazine on the urinary excretion of vitamin C in rats and guinea pigs.] *Archivos del Instituto de Farmacología Experimental*, 1962, 14, 61-64.

Chlorpromazine (3-8 mg/kg/day in rats and 5-20 mg/kg/day in guinea pigs, i. m.) decreased the urinary excretion of vitamin C by 21-30% in rats receiving 150 mg/kg/day of ascorbic acid and by 40-77% in guinea

pigs receiving 300 mg/kg/day of ascorbic acid. The decrease became more marked with time and increasing dosage. Problems in the colorimetric determination of urinary vitamin C are discussed.

Instituto de Farmacología Experimental
Madrid, Spain

1659 Correale, P. Azione della reserpina e dell'iproniazide sulle nuove sostanze imidazoliche del cervello di rana. [Effect of reserpine and iproniazid on the new imidazol derivatives in frog brain.] Bollettino della Società Medico-Chirurgica di Cremona, 1962, 38, 281-282.

Chromatographic determination of 2 imidazol derivatives (acid and amino acid) in acetone extracts of frog brain 24 hours after the end of 5 days' treatment with either reserpine (5 mg/kg/day) or iproniazid (100 mg/kg/day) showed that neither drug produced any significant change in the level of these imidazol derivatives.

Istituto di Farmacologia
Università di Parma
Parma, Italy

1660 Hoffmann, Charles, Frossard, Jacques, Mai-Xuan, Kiem, & Karadavidoff, Isaac. Hydrazines N_1N_2 disubstituées et monoamino oxydase. [N_1N_2 -disubstituted hydrazines and monoaminoxidase.] Annales Pharmaceutiques Françaises, 1962, 20, 539-544.

The authors discuss the synthesis and physical properties of 15 N_1N_2 -disubstituted hydrazines, especially derivatives of isopropylhydrazine, and report briefly that several of these are considerably more active against MAO in vivo than iproniazid, even though lacking in vitro activity (techniques not described). For reasons which remain obscure, dialkylhydrazines seem to attack liver MAO preferentially while those with aromatic substituents are more effective against cerebral MAO activity.

Laboratoires Allard
19 Quai du Port
Nogent-sur-Marne, France

1661 Opitz, Klaus, & Loeser, Arnold. Abschwächung der blutzuckersenkenden Wirkung antidiabetischer Substanzen durch Neuroleptika. [Abolition of the hypoglycemic effect of antidiabetic substances by neuroleptics.] Deutsche Medizinische Wochenschrift, 1962, 87, 105-106.

Determinations of the blood sugar in rats following administration of either dimethylbiguanide alone (300 mg/kg p.o.), dimethylbiguanide plus chlorpromazine (10 mg/kg i.p.), dimethylbiguanide plus chlorprothixene (10 mg/kg i.p.), tolbutamide alone (100 mg/kg p.o.), tolbutamide plus chlorpromazine, tolbutamide plus chlorprothixene, insulin alone (2.0 IU/kg s.c. or 0.2 IU/kg i.v.), insulin plus chlorpromazine or insulin plus chlorprothixene showed that both neuroleptics had a marked hyperglycemic effect which completely abolished the hypoglycemic effects of the other drugs. Experiments with n-butylbiguanide (250 mg/kg p.o.) were inconclusive due to variability of the results. The neuroleptics probably act by inhibiting peripheral glucose catabolism.

Pharmakologisches Institut der
Universität Münster
Münster/Westphalia, Germany

See also 1377, 1408, 1410, 1415, 1490, 1501, 1504, 1533, 1607.

PUBLICATIONS SCANNED BY PSYCHOPHARMACOLOGY ABSTRACTS

This list of publications is in 2 parts: the "core publications" are those containing a relatively large number of psychopharmacology articles. The "other publications" are scanned for the occasional psychopharmacological article they may contain.

CORE PUBLICATIONS

- *ACTA NEUROLOGICA ET PSYCHIATRICA BELGICA
- *ACTA NEUROPSYQUIATRICA ARGENTINA
- *ACTA PHARMACOLOGICA ET TOXICOLOGICA
- *ACTA PHYSIOLOGICA ACADEMIAE SCIENTIARUM HUNGARICAE
- *ACTA PHYSIOLOGICA ET PHARMACOLOGICA NEERLANDICA
- *ACTA PSYCHIATRICA ET NEUROLOGICA SCANDINAVICA
- *ACTAS LUSO-ESPANOLAS DE NEUROLOGIA Y PSIQUIATRIA
- *AGRESSOLOGIE
- *AMERICAN JOURNAL OF MENTAL DEFICIENCY
- *AMERICAN JOURNAL OF PSYCHIATRY
- *ANIMAL BEHAVIOR
- *ANNALES MEDICO-PSYCHOLOGIQUES
- *ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
- *ARCHIVES INTERNATIONALES DE PHARMACODYNAMIE ET DE THERAPIE
- *ARCHIVES OF GENERAL PSYCHIATRY
- *ARZNEIMITTEL-FORSCHUNG
- *BIOCHEMICAL PHARMACOLOGY
- *BOLLETTINO DELLA SOCIETA ITALIANA DE BIOLOGIA SPERIMENTALE
- *BRITISH JOURNAL OF MEDICAL PSYCHOLOGY
- *BRITISH JOURNAL OF PSYCHIATRY
- *BRITISH MEDICAL JOURNAL
- *BULLETIN OF EXPERIMENTAL BIOLOGY AND MEDICINE /TRANSLATION
- *BYULLETEN EKSPERIMENTAL NOI BIOLOGII I MEDITSINY
- *CANADIAN MEDICAL ASSOCIATION JOURNAL
- *CLINICAL MEDICINE
- *CLINICAL PHARMACOLOGY AND THERAPEUTICS
- *COMPREHENSIVE PSYCHIATRY

- *COMPTES RENDUS DES SEANCES DE LA SOCIETE DE BIOLOGIE ET DE SES FILIALES/PARIS/
- *CURRENT THERAPEUTIC RESEARCH, CLINICAL AND EXPERIMENTAL
- *DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT
- *DIA MEDICO
- *DISEASES OF THE NERVOUS SYSTEM
- *ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY
- *ENCEPHALE
- *EXPERIMENTAL NEUROLOGY
- *FARMAKOLOGIYA I TOKSIKOLOGIYA
- *FEDERATION PROCEEDINGS
- *GAZZETTA MEDICA ITALIANA
- *HOSPITAL /RIO DE JANEIRO/
- *JOURNAL OF THE AMERICAN GERIATRICS SOCIETY
- *JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION
- *JOURNAL OF CLINICAL AND EXPERIMENTAL PSYCHOPATHOLOGY AND QUARTERLY
REVIEW OF PSYCHIATRY AND NEUROLOGY
- *JOURNAL OF COMPARATIVE AND PHYSIOLOGICAL PSYCHOLOGY
- *JOURNAL OF MEDICINAL AND PHARMACEUTICAL CHEMISTRY
- *JOURNAL OF NERVOUS AND MENTAL DISEASE
- *JOURNAL OF NEUROCHEMISTRY
- *JOURNAL OF NEUROPSYCHIATRY
- *JOURNAL OF PHARMACEUTICAL SCIENCES
- *JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS
- *LANCET
- *MEDIZINISCHE KLINIK
- *MEDIZINISCHE WELT
- *MODERN DRUGS
- *NATURE

- *NAUNYN-SCHMIEDEBERGS ARCHIV FUR EXPERIMENTELLE PATHOLOGIE UND PHARMAKOLOGIE
- *NEUROLOGIA, NEUROCHIRURGIA I PSYCHIATRIA POLSKA
- *NEURO-PSYCHOPHARMACOLOGY
- *NEW ENGLAND JOURNAL OF MEDICINE
- *NEW YORK STATE JOURNAL OF MEDICINE
- *NORDISK MEDICIN
- *ORVOSI HETILAP
- *PAVLOV JOURNAL OF HIGHER NERVOUS ACTIVITY /TRANSLATION OF ZHURNAL VYSSHEI
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ABBREVIATIONS

AACL	Zuckerman's Affect Adjective Check List	5HTP	5-hydroxytryptophane
ACTH	adrenocorticotrophic hormone	i. a.	intraarterial
ad lib.	free choice	ibid.	in the same place
A. M.	morning	i. e.	that is
AMA	American Medical Association	i. m.	intramuscular
Art.	Article	IMPA	Lorr's Inpatient Multidimensional Psychiatric Scale
ATP	adenosinetriphosphate	i. p.	intraperitoneal
BAL	British antiLewsite	IPAT	Cattell's Institute for Personality and Ability Testing Anxiety Scale
BAS	benzyl analogue of serotonin	I. Q.	intelligence quotient
b. i. d.	twice a day	IU	international unit
BOL	bromolysergic acid diethylamide	i. v.	intravenous
BUN	blood urea nitrogen		
ca.	about	kg	kilogram
CAR	conditioned avoidance response	K _i	Michaelis constant for an inhibitor
CBS	chronic brain syndrome	K _m	Michaelis constant for a substrate
cc	cubic centimeter		
cm	centimeter	lbs	pounds
cm ²	square centimeter	LD	lethal dose
cm ³	cubic centimeter	LSD	lysergic acid diethylamide
CNRS	Centre National de la Recherche Scientifique	μ	micron
CNS	central nervous system	μc	microcurie
COMT	catechol-o-methyl transferase	μg	microgram
cps	counts per second	μl	microliter
CR	conditioned reflex (response)	μM	micromolar
CS	conditioned stimulus	mm	millimicrons
CTD	Climbing Time Delay	M	molar
		ma.	milliamperes
DDT	dichlorodiphenyl trichloroethane	MACC	Motility Affect Cooperation Communication
DOPA	3, 4-dihydroxy-phenylalanine	MAO	monoamine oxidase
DPH	diphosphopyridinenucleotide	MAS	Taylor Manifest Anxiety Scale
DPNH	reduced diphosphopyridine-nucleotide	meq	milliequivalents
		ml	milliliter
ECG	electrocardiogram	mm ²	millimeter
Ed.	editor	mm	square millimeter
ED	effective dose	MMPI	Minnesota Multiphasic Personality Inventory
EDTA	ethylenediaminetetraacetic acid	MSRLP	Multidimensional Scale for Rating Psychiatric Patients
EEG	electroencephalogram		
e. g.	for example	N	normal
ERG	electroretinogram	NEFA	nonesterified fatty acid
et al.	and others	NIMH	National Institute of Mental Health
etc.	and so forth		
FFA	free fatty acid	p	probability
g	gram	PAH	para-aminohippuric acid
GABA	γ-aminobutyric acid	PBI	protein-bound iodine
GABOB	γ-amino-β-hydroxybutyric acid	pH	negative logarithm of the hydrogen ion concentration
HD	hypnotic dose	P. M.	afternoon and evening
5HIAA	5-hydroxyindoleacetic acid	p. o.	by mouth
5HT	5-hydroxytryptamine		

ppm	parts per million	t. i. d.	thrice a day
PRP	Psychotic Reaction Profile	TPN	triphosphopyridinenucleotide
		TPNH	reduced triphosphopyridine-nucleotide
q. i. d.	four times a day	TSH	thyroid-stimulating hormone
refs.	references	U	unit
Rf	ratio of the distance of dissolved substance to solvent distance	UR	unconditioned response
RNA	ribonucleic acid	US	unconditioned stimulus
ru	rat unit	USAF	United States Air Force
s. c.	subcutaneous	USDHEW	United States Department of Health, Education, and Welfare
S. D.	standard deviation	USP	United States Pharmacopoeia
SGOT	serum glutamic oxaloacetic transaminase	USPHS	United States Public Health Service
SGPT	serum glutamic pyruvic transaminase	UV	ultraviolet
sic	exactly as found	VA	Veterans Administration
SOSAI	Springfield Outpatient Symptom and Adjustment Index	viz.	namely
SRA	Science Research Associates	WAIS	Wechsler Adult Intelligence Scale
Suppl.	supplement	WPRS	Wechsler Psychiatric Rating Scale
TH	thyroid hormone		

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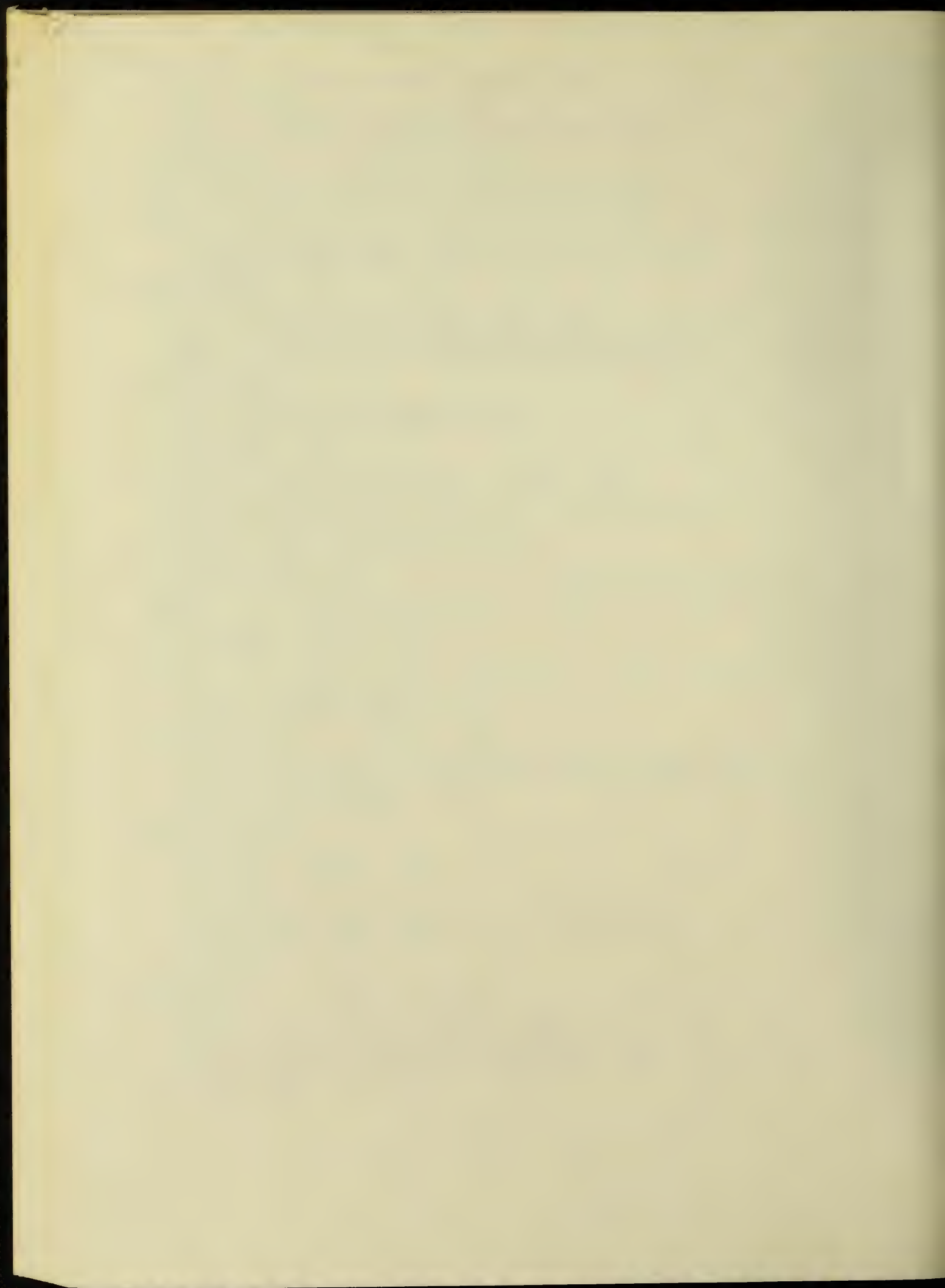
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Psychopharmacology ABSTRACTS

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U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results.

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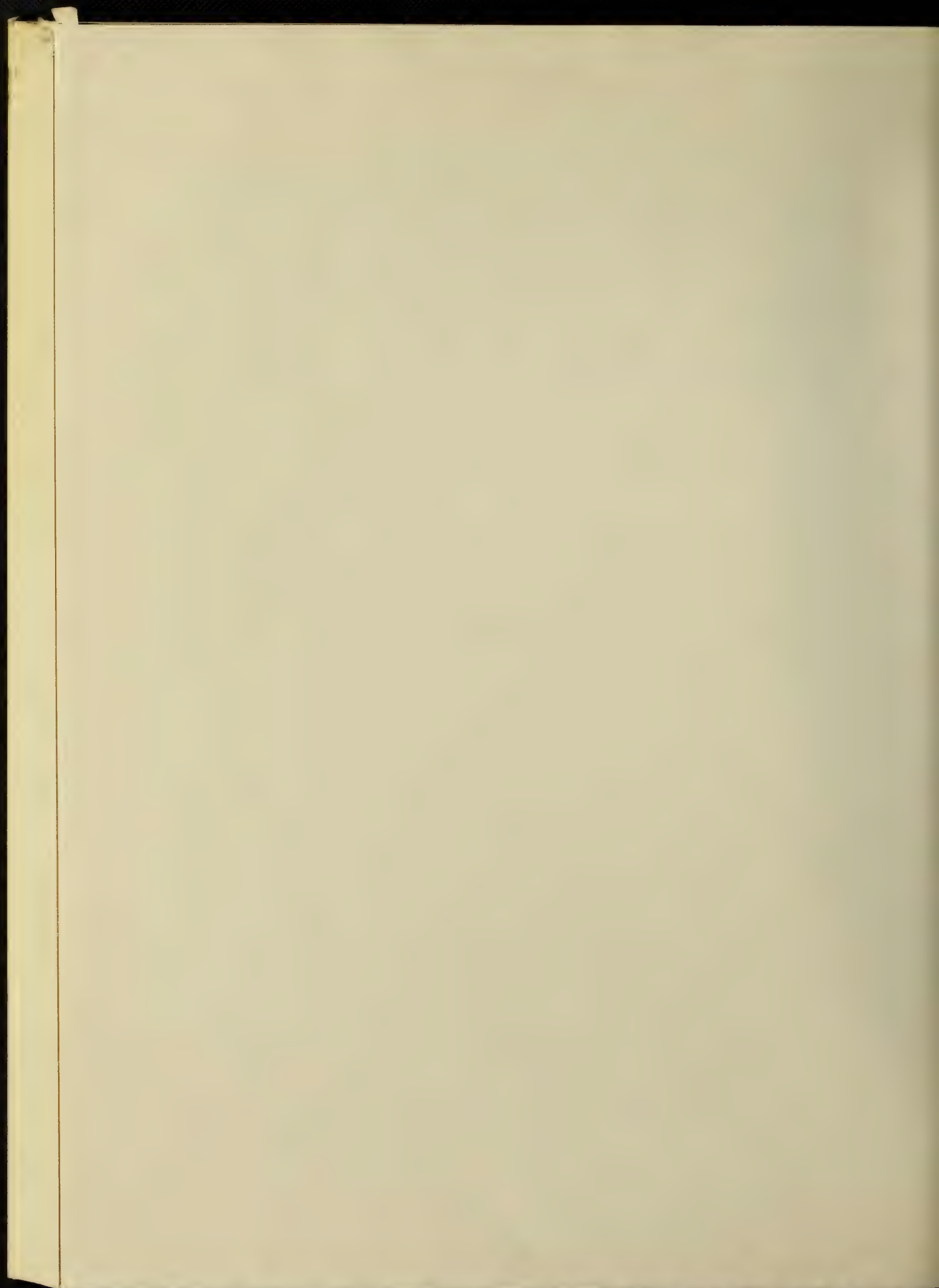
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Bethesda 14, Maryland

PSYCHOPHARMACOLOGY ABSTRACTS

Volume 2, Number 8

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662 Wieser, Stefan, & Baier, Paul. Fortschritte in der Klinik und Therapie des chronischen Alkoholismus. [Advances in the understanding and therapy of chronic alcoholism.] Deutsche Medizinische Wochenschrift, 1962, 87, 150-157.

With respect to the etiology of alcoholism, the authors describe the genetotropic, endocrine and psychogenetic theories, the latter being based on psychoanalysis and psychiatry, as well as on modern learning theory. Various investigations on experimental model situations have indicated that alcohol tends to inhibit those impulses in humans and animals which have their origin in anxiety and fear. In terms of modern learning theory this relief constitutes a reward which leads to repetition and hence to chronic alcoholism. The catabolism of alcohol is reviewed in relation to the use of disulfiram, and particular attention is paid to the treatment of delirium tremens, in which the phenothiazines, reserpine and other tranquilizers have been useful. Favorable prognoses for treatment of the individual patient are to be found in generally good social, familial, economic, and educational levels. Subnormal intelligence, psychopathic tendencies, and hysterical neurotic attitudes are unfavorable factors. (30 refs.)

Universitäts Nervenlinik
Münster, Germany

663 Lüllmann, H. Die Nebenwirkungen der Antiepileptica. [Side effects of antiepileptic drugs.] Arzneimittel-Forschung, 1962, 12, 868-873.

The author surveys clinical literature on the side effects associated with a number of antiepileptic drugs. These include: trimethadione (erythropoietic disturbances, leukopenia, megaloblastic anemia, various psychic disturbances, neurological symptoms, gastrointestinal troubles, and acute intoxication); phenytoin (damage to bone marrow, agranulocytosis, changes in blood picture, psychic disturbances of various kinds, gingival hypertrophy, exanthema, gastrointestinal disturbances); mephentermine (erythro- and leukopoiesis, edema, exanthema, somnolence, epidermal damage, gingival hypertrophy, broncho-

vascular changes); trimethadione (hemopoietic disturbances, agranulocytosis, increased grand mal attacks, disturbances of the central nervous system, damage to sight, kidneys, liver, epidermis); phenacemide (similar to above, also personality changes). Percent frequencies of the various side effects are given, as reported in the literature. (127 refs.)

Pharmakologisches Institut der
Universität Mainz
Mainz, Germany

1664 Arnold, Otto Heinrich. Die Therapie der malignen Hypertonie. [Treatment of malignant hypertension.] Deutsches Medizinisches Journal, 1962, 13, 502-507.

The author reviews the use of drugs for the symptomatic treatment of hypertension. These are classified according to the locale of their action, i.e., the central sympathetic nervous system (meprobamate, reserpine), the sympathetic ganglia (ganglion-blockers), the postganglionic adrenergic fibers (sympathetic inhibitors), the sympatholytics, and the saluretics. Indications, and both relative and absolute contraindications for a variety of drugs falling into the above classes are presented. In malignant cases, when it is urgent to reduce blood pressure in the shortest possible time, guanethidine may be used. In general, and particularly in benign cases, even when these occur in a severe form, the simplest available hypotensive drug should be used, in combination with saluretics together with a salt-free diet (maximum intake, 5-8 g daily). The decision to use hypotensive drugs should be made only after thorough examination of the patients' general condition and family history. (10 refs.)

Medizinische Klinik
Städtische Krankenanstalten
Essen, Germany

1665 Pougetoux, J., Campagnolle, A., & Viader, A. Contribution à un essai critique de classification des drogues psychotropes. [Contribution to a critical attempt to classify psychotropic drugs.]

Journal de Médecine de Lyon, 1962,
No. 1008, 648.

Brief mention is made of RP 1560, levomepromazine, thioproperazine, imipramine and thioridazine in regard to classification based on the evolution of neuromuscular excitability curves, which parallel the plasma sodium/erythrocytic potassium ratio and plasma potassium. (No refs.)

[No address]

1666 Caffey, Eugene M. The use of drugs in outpatient and inpatient psychiatric practice. Virginia Medical Monthly, 1962, 89, 55-59.

Classification of the phenothiazine derivatives based upon "low-dose" and "high-dose" groups is discussed. Various side effects are mentioned and the trend is toward administration of "low-dose" drugs because of relative freedom from undesirable side effects. While drugs have been most helpful, and the phenothiazines most effective in the management of schizophrenic illnesses, the trend should evolve from asking which drug is most effective to whether or not a drug is absolutely essential. Older somatic therapies should not be denied consideration and are frequently useful in combination with drugs. With regard to antidepressants, the side effects of imipramine and the MAO inhibitors include rapid shifting into manic states, marked vascular hypotension and weight gain. Antidepressants can be used with ECT and are also important in general medical practice where they reduce the incidence and severity of angina pectoris and enhance psychomotor activity in rheumatoid arthritis. Much additional study of both the etiology of the disorders treated and the action of the drugs used is necessary. (No refs.)

VA Hospital
Perry Point, Md.

1667 Irvine, J.H. The differential diagnosis of psychalgia and psychophysiologic disease of the locomotor system. Introducing a new classification. Virginia Medical Monthly, 1962, 89, 449-453.

Psychogenic pain is discussed and classified. Psychalgia, (hallucinated pain), a relatively rare condition, should lead to a correct diagnosis of the causative psychosis or severe psychoneurosis. It should be clearly distinguished from pain-producing psychophysiologic phenomena in systems of the body peripheral to the brain. Such phenomena in the locomotor apparatus are exceedingly common and are characterized by pain, stiffness after rest, typical localized areas of nonarticular tenderness, arthralgias, in many cases concomitant with nonrheumatoid disease of the joints, nocturnal cramps in the legs and feet, and stenosing tenosynovitis. Associated psychic symptoms include anxiety, tension, insomnia, fatigue and depression. Precipitating life situations and personality disturbances often based upon underlying resentment combine to produce this syndrome. In severe hypochondriasis the nonarticular tenderness reaches a maximum of distribution and intensity, but usually spares the hands and feet with no evidence of arthritis. Attempts at therapy in fixed hypochondriasis are useless. Medicinal therapy of the psychophysiologic musculoskeletal syndrome is usually of slight value. In cases accessible to psychotherapy or those whose life situation greatly improves, cessation of psychic and physical symptoms and disappearance of nonarticular tenderness have been noted. An illustrative case history was included. (5 refs.)

135 East 65th Street
New York 21, N. Y.

1668 Orgel, Samuel Zachary. The present status of shock or somatic treatment. New York State Journal of Medicine, 1962, 14, 2378-2389.

After a brief historical introduction, the following topics were discussed: insulin coma therapy (technique and selection of patients), subcoma, the convulsive therapies, pharmacologic convulsive treatment, inhalation convulsive treatment with indokon, ECT, electric narcosis, electric sleep, combined insulin-convulsive treatment, indications and results (regarding the affective disorders), manic

depressive psychosis, involutional psychosis, schizophrenia, psychoneuroses, psychosurgery, pharmacotherapy psycholeptics or sedatives, psycho-
naleptics and psychodysleptics or psychoto-
mimetics), psychiatric indications, symptomatic psychoses, alcoholism, drug withdrawal, contraindications, comparison of treatments, present trends and inpatient services. Drugs mentioned include hexafluorodiethyl ether, pentamethylentetrazol, amphetamines, chlorpromazine, reserpine, LSD, ditran, sernyl, pethidine, phenergan, parcol and meprobamate. (34 refs.)

Hillside Hospital
Green Oaks, N. Y.

1669 Flynn, Patrick, & Hirsch, Solomon. Antidepressants and electroshock. American Journal of Psychiatry, 1962, 9, 576-577.

The trend toward replacement of ECT with antidepressant drugs is condemned on the basis that published reports of significant patient improvement due to antidepressant drugs are apparently erroneous. Clinical studies indicate that only 50% of the depressed patients who formerly would have received ECT responded to drugs, whereas the remaining 50% were unresponsive to antidepressants and later experienced successful recovery with a course of ECT. The obvious discrepancy between journal articles and experimental studies may be due to the following: many depressions are self-limiting and may disappear without therapeutic intervention, extraneous factors unrelated to therapy may influence the depression, validity of the rating scale used to evaluate improvement may be insignificant and the absence of thorough follow-up studies may fail to detect relapses. Antidepressants require a 10 week trial to determine drug efficacy, and the resultant side effects may be disastrous. Toxicity has already precipitated withdrawal of 3 such compounds (tryptamine, iproniazid and pheniprazine) from the market. In view of the above information, ECT should hardly be considered obsolete. (9 refs.)

Department of Psychiatry
Dalhousie University
Halifax, N. S.
Canada

1670 Ariens, E.J., & Simonis, A.M. Drug-receptor interaction. Acta Physiologica Pharmacologica Neerlandica, 1962, 11, 151-172.

A comprehensive review of drug-receptor interaction encompasses 3 distinct part-processes (overall metabolism, drug-receptor interaction with drug stimulus, and the relationship between the stimulus induced and the effect obtained), affinity and intrinsic activity (in terms of the Michaelis-Menton equation), the processes concerned with affinity and competition (Van der Waals forces, Lineweaver-Burke reciprocals, etc.), and irreversible and noncompetitive blockade. Copious experimental data illustrates the theories mentioned above. Concentration-response curves and Lineweaver-Burke reciprocals are plotted in terms of competitive and noncompetitive antagonism. Data concerning the following types of compounds is used to illustrate the basic principles of drug-receptor interaction: carcinogens, oxytocin derivatives, parasympathomimetics, sympathomimetics, spasmogens and PABA derivatives. Competitive antagonism, noncompetitive antagonism and irreversible drug blocking action are thoroughly elucidated. (41 refs.)

Pharmacological Institute
R.C. University
Nijmegen, The Netherlands

1671 Knapman, William B. The basic principles of psychosomatic disease. British Journal of Clinical Practice, 1962, 16, 465-473.

Three aims are given relating to psychosomatic disease for the general practitioner: a new classification of psychosomatic disease; establishment of criteria for the identification of psychological symptoms in somatic disease, and elucidation of general principles of treatment in the more commonly recognized psychosomatic

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diseases. The latter are classified under 4 major headings: the physical symptoms in psychological disease which disappear when the mental disease is cured; intermediate disease which includes both mental and physical symptoms of unknown etiology, e.g., anorexia nervosa, alcoholism, epilepsy, migraine, etc; stress symptoms which begin at a time of crisis but subside when the stress is resolved, and finally major psychosomatic disease, e.g., gastric ulcer or ulcerative colitis. A more positive approach in treatment is needed, hypnosis is often valuable, and in some cases "simple" psychotherapy combined with sedation such as amytal and phenobarbital is indicated; ECT is sometimes necessary and leucotomy may be helpful in chronic pain and occasionally in long-standing "closed circuit" disease. The general practitioner should assess the patient since he probably knows the patient best. The existence of free-floating anxiety and hysteria concomitant with physical disease and the physical side of psychosomatic disease must never be forgotten or overlooked in psychiatric treatment. (No refs.)

King George Hospital
Ilford, Great Britain

1672 Luby, Elliot D. Reply to the foregoing. *American Journal of Psychiatry*, 1962, 119, 591. [Letter]

The author of a paper entitled "Model psychoses and schizophrenia" welcomes the hypothesis postulated by a colleague that the weird and terrifying body images experienced by schizophrenics may have their basis in defective screening of afferent inflow, particularly from proprioceptors. Dr. Jensen's comments are particularly pertinent on the relationship between psychopathology and the control and switching of sensory input and attention. Extensive testing of the above hypothesis is anticipated. (No refs.)

Lafayette Clinic
Detroit, Mich.

1673 Burn, J. L. Treatment of addictions.

Lancet, 1962, No. 7247, 151. [Letter]

Special units should be instituted to treat alcoholism, excessive nicotineism and drug addiction in every hospital. The services of specialists are frequently required, along with drugs administered on an in-patient or outpatient basis. Specially designed units will perhaps enable young physicians to develop an interest in the study of addiction. Since a multiplicity of cases of serious addiction are being discovered through the operation of the public-health team and the National Health Service and Mental Health Acts, such restorative facilities are urgently needed to rehabilitate these individuals. (No refs.)

[No address]

1674 Hollister, Leo E. Poisoning due to chemicals and drugs. *Medical Clinics of North America*, 1962, 46, 583-591.

A comprehensive treatise on the role of poisons in society includes the following topics: types of poisons, prevention of poisoning, diagnosis of poisoning and immediate treatment, ridding the patient of poison and removing the poison from the patient's immediate area, specific antidotes for certain poisons (CNS depressants, CNS stimulants, CO₂, salicylates, etc.) and prevention of unpleasant sequelae. A drive is currently underway to widely disseminate information about poisons and their antidotes. Poison centers offer aid to the stricken on a round-the-clock basis. Improved methods of treatment which rely upon mechanical ventilators, hemodialysis and new drugs for sustaining respiration and circulation salvage a considerable number of lives. (14 refs.)

VA Hospital
Palo Alto, Calif.

1675 Shurley, Jay T., & Pokorny, Alex D. Handling the psychiatric emergency. *Medical Clinics of North America*, 1962, 46, 417-426.

The following precepts for handling psychiatric emergency cases are proffered:

definition of the psychiatric emergency, principles of treatment, reassuring conversation, skillful physical intervention, the role of medication (sedatives, minor or major tranquilizers such as chlorpromazine, 50-100 mg) and the need for obtaining assistance from the proper officials by telephone. Psychiatric emergencies common to medical practice include: the suicidal patient, the self-mutilating patient, the violent or disturbed patient, the uncooperative patient who refuses treatment or demands release from the hospital, the dangerous escapee, the manic-stricken patient, the patient who threatens foolish behavior, the addict suffering withdrawal symptoms, the psychotic driver, the patient who appears to be defeated to the point where he no longer defends his life, the psychotic parent of a sick child and the patient about to receive a fatal prognosis. Principles of psychological first aid comprise acceptance of the patient as he is, prompt action, personal human contact to reassure the patient and an overabundance rather than a dearth of aid. (3 refs.)

A Hospital
Oklahoma City, Okla.

1676 Bradley, P. B. Diffuse systems of the brain: physiological and pharmacological mechanisms. *Developmental Medicine and Child Neurology*, 1962, 4, 49-54.

The brain-stem reticular formation is known to control levels of wakefulness and consciousness through an ascending facilitatory influence on higher centers. Anesthetized unrestrained animals are used for studies to determine the influence of drugs on wakefulness and sleep production. Amphetamine and the barbiturates exhibit localized action in the arousal system of the brain-stem. Cholinergics such as physostigmine and atropine evince diffuse action which produces a dissociation between EEG and behavior. The tranquilizers (chlorpromazine) and hallucinogenic drugs (LSD) do not markedly effect levels of wakefulness and exert no direct action on the brain-stem reticular formation. These drugs are concerned with sensory influences on the arousal system, the chlorpromazine having

a depressant effect and LSD facilitating the arousal effects of sensory potentials. These drugs produce their effects by disturbing the relationship between specific and nonspecific afferent pathways in the brain. (15 refs.)

Department of Experimental Psychiatry
Medical School
Birmingham 15, Great Britain

1677 Jensen, S. E. Model psychoses and schizophrenia. *American Journal of Psychiatry*, 1962, 119, 590-591. [Letter]

The hypothesis of an aberrant proprioceptive feedback mechanism operant in both the phencyclidine induced state and chronic schizophrenia is promulgated. Corroboration is offered in the form of previous work on cats with implanted visual, auditory and subcortical electrodes. Responses to a flashing light recorded from the occipital cortex were almost abolished when the animal reduction was also observed in afferent leads from the optic tract and optic pathway, apparently due to a reduction in afferent inflow. Other experimental work indicates that reduction of inflow from one modality with concomitant augmentation of inflow through another modality is probably carried out at the lowest level in the afferent pathway. This evidence offers a new frame of reference from which various psychological anomalies such as sensory deprivation, model psychoses, schizophrenia, conversion hysteria and hypnosis (all conditions predicated upon abnormal input) may be evaluated. Further research on this hypothesis is contemplated with animals given LSD or phencyclidine and schizophrenics undergoing brain surgery. (No refs.)

[No address]

1678 Dundee, John W., & Barron, David W. The barbiturates. *British Journal of Anaesthesiology*, 1962, 34, 240-246.

Clinically efficacious barbiturates are derived from barbituric acid by alterations in the parent nucleus at the 1, 2 and 5, 5'

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positions, and substitutions in the 5 position determine the degree and duration of narcosis obtainable from the following 4 distinct chemical groups: barbiturates (or oxybarbiturates), methylated oxybarbiturates, thiobarbiturates and methylated thiobarbiturates. Classification is predicated upon duration of drug action, i.e., ultra-short, short, medium, intermediate and long acting barbiturates. Replacement of both H atoms on the 5-C by alkyl or aryl groups confers hypnotic properties on the barbiturates. Halogenation of the alkyl substituents increases drug potency and intensity of action. Long acting barbiturates are typified by phenobarbital and barbital, medium acting by amylobarbitol, and rapidly acting by thialbarbital, hexobarbital and enallylpropymal. Sulphuration results in a compound which has highly effective soporific properties. 1-Methylation of a barbiturate or thiobarbiturate confers convulsive properties which are manifested as anomalous skeletal muscle activity. Certain side chains on the 5-C increase the incidence of coughing and hiccoughing for unknown reasons. Compounds of the barbiturate group commonly used in anesthesia are presented in tabular form along with all relevant chemical data. (7 refs.)

Department of Anaesthetics
The Queen's University of Belfast
Northern Ireland

1679 Schindel, L.E. Placebo in theory and practice. *Antibiotica et Chemotherapia, Advances*, 1962, 10, 398-430.

This general discussion of the placebo starts with its historical origins and theorizes that most medication up to and including today is actually based on placebo response. Pure and "impure" placebos are differentiated in that impure is an active substance administered under false premises and/or in insufficient dosage. Other topics covered are the placebo effect, magic, suggestion, conditioning, the simple blind test, the double-blind test, placebo reactors and nonreactors. Studies in which placebos are compared with tranquilizers and energizers have often cast doubt upon the drug's utility and conversely, placebos

sometimes caused side effects. The benefits to patients from placebo surgery are also discussed. (92 refs.)

P.O.B. 7071
Jerusalem, Israel

1680 Adler, T.K. Physical-chemical and pharmacological properties of azaindoles. *Proceedings of the Western Pharmacology Society*, 1962, 5, 17. [Abstract]

Monoazaindoles produce acute biological effects which resemble those of indole, i.e.: 4-, 5-, and 6-azaindole [dosage unspecified] except considerably augmented convulsive action in mice. Both 7-azaindole and benzimidazole (3-azaindole) produce paralysis in mice. A mixture of stimulant and depressant effects is evinced by isoindazole (2-azaindole). Incorporation of an iso-electronic N atom in place of a methine group in indole confers basic properties on the structure and decreases the oil/water distribution ratio. (No refs.)

Department of Pharmacology
U.C. Medical Center
San Francisco, Calif.

1681 Cameron, D. Ewen. Psychiatry and general office practice. *American Practitioner*, 1962, 13, 307-316.

The growing importance of the family doctor in dealing with mental disorders due to more precise measures of diagnosis and treatment which are more effective, precise less time consuming and more readily handled, is discussed. This trend is reflected in training centers for those in general practice. The recognition of psychiatric illness, tension and anxiety components, is most frequently done by the family doctor. The milder depressions are presently well within the competence of the general practitioner thanks to drugs such as imipramine and the MAO inhibitors. The role of tranquilizers is self-evident. Finally the "therapeutic" role of the practitioner is emphasized. (No refs.)

Allen Memorial Institute
McGill University
Montreal, Quebec
Canada

1682 Weiner, Myron F. The treatment of depression. *Medical Times*, 1962, 90, 47-50.

Situational, dependent and psychotic depressions, the latter including involuntional melancholia, are exemplified and discussed. The difficulty of treating the compulsive personality in psychotic depression is stressed. The utility of tranquilizers, antidepressants and psychotherapy as well as the great effectiveness of ECT in hospitalized patients are reviewed. Drugs cited as particularly useful include phenelzine, imipramine, chlorpromazine and chlordiazepoxide. (6 refs.)

Department of Psychiatry
University of Texas
Southwestern Medical School
Dallas, Tex.

1683 Dagnall, Phyllis. Emergency treatment of poisoning. *Lancet*, 1962, No. 7232, 746 [Letter]

A physician advocates the addition of a green or blue dye to barbiturate preparations to facilitate immediate identification in cases of barbiturate poisoning. Comatose patients in particular would benefit from such a device. Development of a dye which is metabolized to a colorless state before reaching the urine would be optimal, since social and aesthetic motivation would probably preclude extensive drug usage if green urine was passed after drug ingestion. (No refs.)

Royal West Sussex Hospital
Chichester, Sussex
Great Britain

1684 Edwards, Griffith. Alcoholism as a public health problem in the U.S.A. *Lancet*, 1962, No. 7236, 960-961.

An Englishman reviews the concept of alcoholism and its treatment in the U.S.A. Alcoholism is construed as a social problem, and in the past, legislation was directed toward controlling it, but such laws met with little success. The disease is currently treated as a separate entity apart from

existing medical or psychiatric institutions. Group therapy, the establishment of halfway houses designed to elevate the derelict above the skid row environment, teaching healthy attitudes toward alcohol as a preventive measure, state programs for rehabilitation, specialized treatment centers in all major cities, and various programs directed toward prevention have all been instituted to curtail the problem. The combined efficacy of such a comprehensive plan of attack must be thoroughly investigated before any facsimile of the plan is adopted for Great Britain. (12 refs.)

Maudsley Hospital
London, SE 5, Great Britain

1685 Macgregor, A.G., & Perry, W.L.M. Detection of drug toxicity. *Lancet*, 1962, No. 7244, 1406. [Letter]

A previous letter intimated that the antibiotics triacetyloleandomycin and erythromycin have been withdrawn from the British market due to hepatotoxicity. These drugs have not been withdrawn. However, the list of drugs which have been banned due to unpredicted and undesirable toxicity includes thalidomide, triparanol, zoxazolamine, furaltadone, diathazanine and amphenidone. All of these drugs have evidenced intolerable toxicity. (No refs.)

University of Aberdeen
Aberdeen, Great Britain

1686 Macgregor, A.G., & Perry, W.L.M. Detection of drug toxicity. *Lancet*, 1962, No. 7241, 1233-1234. [Letter]

The thalidomide debacle precipitated an acute awareness of drug teratogenicity among members of the medical profession. Stringent legislative controls should be instituted to regulate the marketing of new drugs. Toxic effects are divisible into 3 categories: those which have occurred before that can be detected by a known test in animals, those which are known but for which no animal test has been devised

and those which have not occurred before. Teratogenicity is detectable in rabbits while agranulocytosis, aplastic anemia, hepatotoxicity and carcinogenicity fall into category 2, and future nebulous hazards constitute category 3. Unpredicted and undesirable toxicity has accounted for withdrawal of the following drugs from the market: thalidomide, triparanol, zoxazolamine, furaltadone, diathazanine and amphenidone. Intolerable toxicity has also been observed with triacetyloleandomycin and erythromycin. Several proposals have been suggested to formulate groups designed to study various types of drug toxicity. Bureaucratic inertia has precluded realization of these proposals. It is imperative that adequate information about the therapeutic efficacy of new drugs be made available to physicians. A plea is promulgated for the organized accumulation of information about drug toxicity and efficacy, so control measures may be based on knowledge rather than ignorant supposition. (9 refs.)

University of Aberdeen
Aberdeen, Great Britain

1687 Merriman, B. Alcoholism. *Lancet*, 1962, No. 7241, 1238-1239.

The fact that England has 500,000 alcoholics out of a population of 50 million people indicates a crying need for some definitive effective program of rehabilitation. The public must be persuaded that alcoholism is an urgent problem and a disease entity rather than a condition of simple habitual drunkenness. Alcoholism apparently involves a chronic inability to abstain, so-called "inveterate alcoholism", resulting in CNS sensitization to a constant relatively low blood alcohol concentration called delta alcoholism, which fails to produce acute intoxication but is progressively destructive to bodily functions and social relationships. There is a current tendency for the alpha alcoholic (purely psychological dependence on alcohol or problem drinking to relieve emotional tension) to progress to delta alcoholism rather than the more familiar gamma alcoholism. Public opinion must be educated to accept alcoholism as a disease entity in order to

cope with the problem on a national scope. (No refs.)

[No address]

1688 Harris, E. L. Detection of drug toxicity. *Lancet*, 1962, No. 7242, 1305.

A physician is aghast at the rather dogmatic assertion of Macgregor and Perry that drug teratogenicity will no longer endanger mankind since the development and application of testing procedures in rabbits for detecting teratogenicity in new pharmacological compounds. Such optimism is apparently premature, and extensive research in developing infallible screening methods is indicated before we can safely say that potential drug teratogenicity will invariably be detected before a drug reaches the market. (No refs.)

Nicholas Research Institute Ltd.
Slough, Bucks
Great Britain

1689 Pliess, G. Thalidomide and congenital abnormalities. *Lancet*, 1962, No. 7239, 1128-1129. [Letter]

The Wiedmann syndrome (thalidomide syndrome) consisting of characteristic congenital anomalies resulted in 14 instances from thalidomide ingestion by mothers during the 1st trimester of pregnancy. The teratogenic factor apparently interferes with normal biochemical processes which govern the development of mesodermal structures. Typical extremity malformations probably originate during the scleroblastemal stage. The precise anomalies manifested should theoretically correspond to the period of development during which the noxious factor was administered. Coelomic malformations result from interference with the critical determination phases of the mesenchymal derivatives, predominantly of the lateral and intermediate mesoderm, rather than by directly affecting the organ anlage. Experiments with thalidomide administered to pregnant rats have indicated that the drug does not exert teratogenic effects in rats. Malformations of exogenous origin

re genotype-phase-and-factor specific.
Drug-induced fetal malformations could be
avoided if women would refrain from ingest-
ing drugs for at least 9 weeks after a period
has been missed. (No refs.)

Pathological Institute
University of Hamburg
Hamburg, Germany

1690 Smythies, J.R. Adrenaline and
schizophrenia. *Lancet*, 1962, No. 7233, 802.

To clarify his viewpoint on the "adrenaline
hypothesis" of schizophrenia, a physician
expressed the opinion that schizophrenia
may be associated with a general disorder
of O-methylation, and a portion of this dis-
order may affect intracerebral epinephrine
as well as tryptamine and serotonin. Recent
double-blind studies in Czechoslovakia
indicate that adrenochrome administered
sublingually produces psychotic reactions
and marked EEG changes. It is conceivable
that local production of adrenochrome
occurs in schizophrenia. The original
hypothesis that schizophrenia rests on a
disorder of methylation has been corroborat-
ed by subsequent experimental evidence
such as the fact that epinephrine is normally
metabolized by O-methylation while mes-
saline is metabolized by O-demethylation,
methionine coupled with iproniazid admin-
istered to schizophrenics produces symp-
toms of increased severity, and psycho-
mimetic drug potency is correlated with
ability to potentiate peripheral effects of
epinephrine since most psychotomimetics
act as central stimulants of the sympathetic
nervous system. (7 refs.)

Department of Psychological Medicine
University of Edinburgh
Edinburgh, Scotland

1691 *Lancet*. Thalidomide and pregnancy.
Lancet, 1962, No. 7248, 204. [Editorial]

In a parliamentary discussion, Baroness
Summerskill sought permission from the
government for women who had definitely
received thalidomide during pregnancy to
be granted the legal right to have their
pregnancies terminated. The Lord Chancellor
cited a law enacted in 1938 which stated that

termination of pregnancy may be obtained
legally only if said pregnancy seriously
endangers the mental health of the mother.
Thalidomide was administered primarily
to women of nervous character who
required sedation, thus indicating a certain
degree of mental instability. The act of
abortion may be performed legally only
for the purpose of preserving the life or
mental or physical health of the woman in
question. (No refs.)

7 Adam Street
Adelphi
London W.C.2, Great Britain

1692 Busch, Harris, Adams, Helen, &
Muramatsu, Masami. Effects of alkylating
agents and thioacetamide on nuclear
metabolism. *Federation Proceedings*,
1962, No. 5323, 1093-1096.

A paper dealing primarily with the effects
of alkylating agents and thioacetamide on
nuclear and microsomal RNA content also
includes a brief discussion on phenothiazine
uptake in nuclear components. The
implication of RNA as a vital information
agency in memory has suggested the
possibility that nucleolar phenothiazine
concentration may interfere with the
specific types of RNA which are essential
to the memory process. Purified
preparations of brain nucleoli will be
required for further investigation. (17
refs.)

Department of Pharmacology and
Biochemistry
Baylor University College of Medicine
Houston, Tex.

1693 Spiers, Alexander L. Drug-induced
malformations in the fetus. *American
Heart Journal*, 1962, 5, 717-718.

A considerable body of information culled
primarily from the Continent has established
a definite correlation between ingestion of
thalidomide during the 1st trimester of
pregnancy and resultant fetal anomalies.
Characteristic thalidomide induced aberra-
tions include gross limb defects, cardiac
malformations and gastrointestinal

abnormalities. Teratogenicity affects tissues of mesenchymal origin, but extensive research will be necessary to determine the origin of deleterious effects more precisely. The incidence of thalidomide defects correlated rather closely with the areas in which the drug was freely obtainable. About 3,000 afflicted babies were born in West Germany alone. The tragedy has precipitated a widespread awareness of potential teratogenicity in new drugs, and testing procedures will henceforth be required before a new drug may be marketed. Drugs should be used with the utmost caution in pregnancy to prevent repetition of the thalidomide disaster. (8 refs.)

Stirling Royal Infirmary
Stirling, Scotland

1694 Meyer, Joachim-Ernst. Prominent trends in German psychiatry. *South African Medical Journal*, 1962, 2, 150-152.

German psychiatry essentially originated with the dictums of Kraepelin and progressed to encompass the catholic concepts of Sigmund Freud. Psychiatric research has been based upon the concept of phenomenology as introduced by Karl Jaspers which has recently been enriched by the addition of the concepts of gestalt psychology and Jung's depth psychology. Existential analysis added new depth and dimension to psychiatry when promulgated by Martin Heidegger. Genealogy has become obsolete due to the political implications inherent within its tenets. Biochemical research on the endogenous psychoses flourishes in present day Germany, along with concomitant development of new drugs. Neurophysiology provides a sound basis for a considerable amount of significant research. Recent events such as war neurosis, cerebral atrophy from nutritional deficiency and psychic trauma from concentration camp sojourns have exerted a profound effect on contemporary German psychiatry. Insulin shock therapy, ECT, imipramine and the MAO inhibitors, haloperidol and orphenadrine are all important constituents in the modern therapeutic armamentarium. (20 refs.)

Nervenklinik
University of Munich
Munich, Germany

1695 Weiner, Herbert. Narcotic addiction. In: Conn, Howard F. [Ed.] *Current Therapy*. Philadelphia: W. B. Saunders, 1962. Pp. 528-531.

Misuse of addicting drugs, with concomitant psychopharmacological effects on motivation affect and psychological organization, often culminates in addiction. A variety of secondary gains predispose toward addiction under propitious circumstances. The role of the physician in narcotic addiction is exceedingly difficult, especially when the addict is a fellow physician or nurse. Drug withdrawal should invariably be carried out in a hospital setting in order to provide maximal supervision of abstinence symptoms while controlling drug intake. Positively directed motivation is an essential factor in withdrawal and rehabilitation of drug addicts. Mild cases of abstinence syndrome may be treated by attention to fluid and dietary requirements, paraldehyde sedation and chlorpromazine or promazine (100-200 mg every 4 to 6 hours parenterally). Oral methadone may be substituted for any of the opiates in cases of more intense addiction. While it is habit forming, its abstinence syndrome is far less severe and abhorrent to the patient. Doses of methadone are reduced by successive increments over a period of 8-10 days once a dose level has been established to control initial symptoms. Phenothiazines should be used with caution since they exert potentiating effects upon opiates. Psychotherapy should be instituted once recovery from withdrawal effects has been observed. (No refs.)

Albert Einstein College of Medicine
New York City, N. Y.

1696 Merritt, H. Houston. Parkinson's disease (paralysis agitans). In: Conn, Howard F. [Ed.] *Current Therapy*. Philadelphia: W. B. Saunders, 1962. Pp. 534-536.

Parkinson's disease (paralysis agitans), caused by diffuse damage to basal ganglia and cerebral cortex, is a progressive disorder characterized by masklike facies, cogwheel muscle rigidity and gait abnormalities. Treatment consists of palliation,

based principally on belladonna-like compounds and physiotherapy. Today, the belladonna alkaloids have largely been replaced by synthetic compounds like trihexyphenidyl (6-20 mg), benztropine (0.5-6 mg), procyclidine (7.5-20 mg), ethopropazine (100-600 mg) and cycrimine (3.75-15 mg). All forms of physiotherapy are of considerable benefit, both in motivating patients and in muscle relaxations. Various surgical ablation procedures performed have frequently resulted in a reduction in the severity of rigidity and tremor with little or no evidence of weakness. Gratifying results have been obtained in patients under 60 years of age with symptoms localized to 1 side of the body. (No refs.)

Presbyterian Hospital
New York City, N. Y.

1697 Brill, Norman Q. Neuroses. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W. B. Saunders, 1962. Pp. 539-541.

Neuroses are treated by psychotherapy and somatotherapy. Supportive psychotherapy involves the utilization of reassurance, encouragement and advice, while expressive psychotherapy deals with dynamic exploration of the psychic origins of neurosis through the techniques of emotional catharsis, corrective emotional experience, clarification, interpretation and the free association upon which psychoanalysis is predicated. Factors which determine the type of psychotherapy include diagnosis, goal of treatment, external precipitating stress, ego strength and motivation, etc. Somatotherapy consists primarily of drugs, CO₂ inhalation, ECT, insulin shock therapy and lobotomy, which is utilized only as a last resort. (No refs.)

University of California School of
Medicine
Los Angeles, Calif.

1698 Eckenhoff, James E. Opiate poisoning. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W. B. Saunders, 1962. Pp. 661-663.

Therapy for poisoning due to overdoses of opium derivatives (morphine) and synthetic analgesics such as meperidine, alpha-prodeine and anileridine includes immediate establishment of adequate pulmonary ventilation and circulatory support followed by determination of the cause of coma, evaluation of the depth of depression and establishment of a tentative prognosis. Drug therapy involves specific antagonists for opiate poisoning such as nalorphine and levallorphan. Deep coma responds to injections of pentetrazol, picrotoxin and methyl-ethyl-glutarimide, and relatively mild narcotic depression may be ameliorated by nikethamide, ephedrine, caffeine and sodium benzoate. Apneic infants may benefit from administration of the narcotic antagonists. Additional beneficial therapy includes aspiration of stomach contents, catheterization, and tracheal aspiration with special emphasis on oral hygiene. (No refs.)

School of Medicine
University of Pennsylvania
Philadelphia, Pa.

1699 Ryder, Henry W. Acute barbiturate poisoning. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W. B. Saunders, 1962. Pp. 660-661.

Acute barbiturate poisoning is to be treated as follows: remain with the patient until consciousness is regained, keep the airway open and gas exchange adequate, observe the vital signs during adequate ventilation, lavage the stomach, transfer the patient to the recovery room if vital signs are normal, administer phenylephrine and levarterenol if the patient is in shock, review the mechanisms by which death is caused from barbiturate poisoning and maintain the patient's general condition until definite signs of recovery are observed. (No refs.)

Deaconess Hospital
Cincinnati, Ohio

1700 Hoffer, A., & Osmond, H. Adrenaline and schizophrenia. Lancet, 1962, No. 7251 643-644.

Evidence is presented which suggests that 3 papers from NIMH which purportedly fail to vindicate the adrenochrome-adrenolutin theory of schizophrenia neither support nor confute the hypothesis that schizophrenia is characterized biochemically by increased conversion of adrenochrome to adrenolutin, a trihydroxy indole with toxicity which approximates that of adrenochrome, which is converted to 5:6 dihydroxy-N-methyl indole, a nontoxic substance. Excess epinephrine is metabolized to adrenochrome, an overabundance of which is present in schizophrenics. No direct correlation has been obtained experimentally, but the NIMH variables hardly lend themselves to a carefully controlled study. It is unlikely that a typical group of normal controls includes American males who drink 1 cup of coffee per day and smoke 1 1/2 cigarettes daily. La Brosse, Mann, and Kety are also guilty of perpetrating the following misconceptions: the hypothesis that dextro-epinephrine is probably inert metabolically; the addition of ascorbic acid, a known antioxidant, to every 100 ml of epinephrine solution despite the fact that it will undoubtedly hinder or prevent the conversion of epinephrine to adrenochrome and the fact that epinephrine injections will probably reduce epinephrine secretion from the adrenal medulla. Esoteric techniques are required to isolate adrenochrome or its metabolites from the urine. Attschule (1961) found aminochromes in schizophrenic urines, in experiments which may prove crucial in ultimately establishing the adrenochrome-adrenolutin hypothesis. (10 refs.)

Department of Public Health
University Hospital
Saskatoon, Saskatchewan
Canada

1701 James, L. S. Apgar Scoring System. *Developmental Medicine and Child Neurology*, 1962, 4, 444.

Critical comments by Dr. Crawford on the Apgar Scoring System for neonates are partially refuted, including the fact that minimally depressed infants evince an absence of muscle tone. Rather, hypertonicity may be observed in the initial stages of asphyxia, particularly with acute trachial

obstruction. Drug depression due to promethazine, chlorpromazine and barbiturates, however, results in characteristic absence of muscle tone. The existing Apgar rating scale will doubtlessly undergo modification as emphasis is placed upon the changing physical signs which typify early readjustment of the newborn. The veracity and detail of these observations are far more significant than the criteria by which they are scored to categorize them for future statistical analysis. Medical data is unfortunately not ideally suited for mathematical treatment. (No refs.)

Presbyterian Hospital
622 West 168th Street
New York 32, N. Y.

1702 Hohman, Leslie B. Psychoses: Mental depression. In: Conn, Howard F. [Ed.] *Current Therapy*. Philadelphia: W. B. Saunders, 1962. Pp. 544-546.

Symptoms of depression are divisible into 3 categories: mood disturbance, biological, physiological or mechanical changes, and disturbance in content. Psychotherapeutic intervention in the form of nursing, support, encouragement and suggestion is ineffective. Psychoanalysis yields only very slight amelioration of symptoms. Physical treatment includes ECT and insulin shock therapy, imipramine, reserpine, phenothiazine derivatives, chlordiazepoxide, meprobamate and iproniazid. Frequently, ECT is listed as the therapy of choice since it provides rapid improvement, minimizes the danger of suicide, reduces hospital costs and relieves acute unhappiness and suffering more readily. (No refs.)

Duke University
Durham, N.C.

1703 Brand, Leonard, & Mark, Lester C. Why use analeptics? *Bulletin of the N. Y. Academy of Medicine*, 1962, 38, 702-704.

Analeptics such as pentetrazol, nikethamide, bemegride and methyphenidate have been used in 3 general areas: in depression or coma of unknown etiology, in severe depression from gross drug overdose or poisoning (i.e., barbiturate poisoning) and

n moderate depression resulting from therapeutic doses of drugs including anesthetics. Analeptic drugs should never be utilized in these situations. In lieu of anesthetics, good recovery room care including careful attention to airway management, maintenance of adequate ventilation, support of circulation and prevention of infection offers the highest rate of recovery with the lowest incidence of complications. Analeptics should never be used to supplement or substitute for good postoperative medical and nursing care. (No refs.)

Department of Anesthesiology
Columbia University College of Physicians
and Surgeons
New York, N. Y.

704 Fouks, L., Laine, Mathis, Ferrant, Riou, & Boucher. Rapport sur l'essai clinique de la dixyrazine. [Report on the clinical trial of dixyrazine.] *Annales Médico-Psychologiques*, 1962, 1, 120, 636-637.

Dixyrazine, a methylated phenothiazine, is similar to levomepromazine in depressive and neurotic states because of its anxiolytic activity. It diminishes nervous tension and excitability. Its side effects are essentially those of piperazine-substituted phenothiazines (akinesia and psychomotor syndrome); these are minimal and easy to correct. The antihallucinatory and antipsychotic activity of dixyrazine is quite weak and it seems best used in cases of instability and character disorder. (No refs.)

[No address]

705 Fouks, L., Lefèvre, Laine, Mathis, Ferrant, Riou, & Boucher. Essai clinique de la trifluopérazine. [Clinical trial of trifluoperazine.] *Annales Médico-Psychologiques*, 1962, 1, 120, 636.

Trifluoperazine is recommended as the best presently available neuroleptic, because of its antihallucinatory and antipsychotic properties and easily managed side effects. (No refs.)

[No address]

1706 Blaya, Marcelo. O uso de tranqüiladores na clinica. [The clinical use of tranquilizers.] *Actas Luso-Españolas de Neurologia y Psiquiatria*, 1962, 21, 153-158.

Tranquilizers are classified into 5 categories: Rauwolfia derivatives, phenothiazine derivatives, diphenylmethane (benactyzine) derivatives, propanodiolics and miscellany. A table of side effects (e.g., agitation, agranulocytosis) for 14 popular tranquilizers (e.g., chlórdiazepoxide, reserpine, meprobamate) is also presented. Promazine is favored in psychotic syndromes, while in neurosis where anxiety is the main feature meprobamate is preferred. (7 refs.)

Av. João Pessoa, 925
Porto Alegre
Rio Grande do Sul
Brazil

1707 Linke, H. Kritik der Therapie: Nebenwirkungen und Gefahren der Anwendung psychotroper und schmerzstillender Pharmaka. [Critique of therapeutics: side effects and dangers of psychotropic and analgesic drugs.] *Deutsches Gesundheitswesen*, 1962, 17, 1095-1101, 1146-1156.

A classification of psychotropic and analgesic drugs based on their affinities for various parts of the nervous system is presented. Side effects are also discussed. The main classes are: neuroleptics; tranquilizers and ataractics; thymoleptics; psychotonics, and analgesics. The great dangers of misuse and addiction are pointed out, particularly in view of the pressures of modern living, the drive to increase individual living standards, the advertising by pharmaceutical houses, and the unwillingness of the overworked physician to deprive a suffering patient of the means of alleviating his pains or tensions. East Germany has gone far in the direction of passing laws for the provision of correct information on the properties of drugs, and for the control of their production. However, the physician owes it to his patient to understand his psychic needs and to treat these not only by drugs, but also by other means. (131 refs.)

Medizinische Klinik
Medizinische Akademie
Magdeburg, Germany

1708 Briggs, Michael H. Possible relations of ascorbic acid, ceruloplasmin and toxic aromatic metabolites in schizophrenia, New Zealand Medicine Journal, 1962, 61, 229-236.

Numerous experimental studies have corroborated the fact that ceruloplasmin levels are higher in acute than in chronic schizophrenia, while both groups evince significantly higher plasma levels than normal subjects. The increased concentration of ceruloplasmin in schizophrenics catalyzes the oxidation of ascorbate to dehydroascorbate, and the preferential oxidation of ascorbate prevents oxidation of circulating amines. Schizophrenics, therefore, will exhibit lower blood ascorbate levels than normal persons, even when an adequate dietary supply of the vitamin is supplied. Schizophrenics tend toward hypercupremia which in turn precipitates a form of hypovitaminosis C. Since ascorbic acid activates the liver enzyme p-hydroxyphenylpyruvic oxidase, the diminished ascorbate levels should result in a corresponding decrease in the extent of aromatic amino acid metabolism by the phenylalanine oxidase system. With partial inhibition of this pathway, aromatic amino acids are metabolized by an alternate pathway which favors increased epinephrine synthesis. The major urinary metabolite of epinephrine, 3-methoxy-4-hydroxymandelic acid, is present in significantly greater concentration in the urine of schizophrenics than in normal urine. It is conceivable that an abnormal metabolite of epinephrine which structurally resembles the psychotomimetic compounds accumulates and exerts toxic activity. It seems improbable that any drug therapy will cure chronic schizophrenia since prolonged action of these toxins on brain tissue has probably induced the type of irreversible cellular changes observed in experimental animals maintained in a state of vitamin C deficiency. Most major psychotherapeutic drugs (chlorpromazine, reserpine, isocarboxazid, etc.) used to treat schizophrenia are capable of altering brain amines related to epinephrine and serotonin and these changes are compatible with the hypothesis that toxic epinephrine metabolites induce schizophrenic brain changes. (67 refs.)

Victoria University of Wellington
Wellington, New Zealand

1709 Austarheim, Kristen. Depersonalisasjon, saerlig ved endogene depresjoner. [Depersonalization, particularly in endogenous depressions.] Nordisk Medicin, 1962, 68, 1159-1161.

In making a correct diagnosis of depression, it must be remembered that a feeling of unreality is not necessarily a schizophrenic symptom, but may be merely a general psychopathological reaction type like anxiety, phobia, or conversion. Emphasis is placed on its possible presence in endogenous depressions, in which the symptoms may be combined with withdrawal. Correct diagnosis is especially important so that anti-depressants may be prescribed in such cases. (27 refs.)

Vestlandets nervesanatorium Solli
Nestun, Norway

1710 Lingjaerde, Odd. Klassifisering av nyere psykofarmaka. [Classification of new psychotropic drugs.] Nordisk Medicin, 1962, 68, 1172-1174.

The following classification was outlined:
A. Neuroleptics (major tranquilizers), including phenothiazine derivatives, phenothiazine-related drugs and others; B. Minor tranquilizers, including substituted alcohols (meprobamate, emylcamate), diphenylmethane derivatives, and others; C. Anti-depressants (thymoleptics), including MAO inhibitors and non-MAO inhibitors; D. Psychotonics (psychoanaleptics and psychostimulants), e.g. methylphenidate; and E. Psychotomimetics (psychodysleptics), e.g. LSD. (12 refs.)

[No address]

1711 Nordenfelt, Olof. Fenacetinmissbruk i en svensk industri. Kliniska synpunkter. [Phenacetin abuse in Swedish industry. Clinical considerations.] Nordisk Medicin, 1962, 67, 756.

Information on 86 deaths due to kidney damage caused by phenacetin is reviewed. The chief reasons for seeking medical aid on the part of phenacetin abusers are shortness of breath and fatigue. Anemia and renal insufficiency were often diagnosed clinically and commonly after 1-4 months the patients died in uremia. (No refs.)

[No address]

1712 Kasanen, A. Fenacetinproblemet i Finland. [The phenacetin problem in Finland.] *Nordisk Medicin*, 1962, 67, 755-756.

About 10% of factory workers, 34% of patients with kidney damage and 16% of others abuse sedatives in Finland. The incidence of papillitis necroticans has risen and about 60% of the cases are phenacetin users. Liver damage was also noted in some cases at autopsy, and changes are regularly seen in the EEG. (No refs.)

[No address]

1713 Björkman, Sven Erik. Njurskador genom fenacetinmissbruk. [Kidney damage due to phenacetin abuse.] *Nordisk Medicin*, 1962, 67, 755.

Prophylaxis against kidney damage caused by phenacetin is advocated, especially since the mechanism of this renal damage is unknown. (No refs.)

[No address]

1714 Naess, Knut. Barbitursyrefri hypnotica. [Barbiturate-free hypnotics.] *Nordisk Medicin*, 1962, 67, 734-735.

After discussing the disadvantages of barbiturates, the author remarks on glutethimide, methypylon, ethinamate, chlorprothixene and thalidomide. The author warns against the injudicious introduction of new agents, as witnessed by the thalidomide tragedy. This is especially true since all of these agents are potential means of suicide. (No refs.)

[No address]

1715 Janssen, Paul. Zur Chemie morphinartiger Körper. [The chemistry of morphine-like substances.] *Anaesthesist*, 1962, 11, 1-7.

The structure of the piperidine derivatives is discussed, and a table presented in which the pharmacological properties of morphine, pethidine, phenoperidine, dextromoramide, pirinitramide, and diphenoxylate are compared. The important chemical features which are relevant to pharmacological properties are described for all known morphinelike analgesics. In view of their chemical similarity, these drugs are believed to act by "fitting" to a specific 3-dimensional receptor, probably located in the thalamus. (24 refs.)

Research Laboratory
Beerse, Belgium

1716 Quadbeck, G. Blut-Hirnschranke und Hirnnahrung. [The blood-brain barrier and cerebral nutrition.] *Medizinische Wochenschrift*, 1962, 104, 24-26.

The concept of the blood-brain barrier as a functional rather than anatomic entity is discussed and the possibility of affecting cerebral transport mechanisms by means of pharmacological agents is pointed out. A decrease in barrier activity as can be produced by aminophyllin, nicotinic acid, reserpine, tetrabenazine, prothipendyl, chlorpromazine, chlorprothixene, triflupromazine and perphenazine permits the needs of the brain to be met by simple diffusion. However, as shown by experiments in mice, glucose uptake by the brain is not increased immediately by these agents, a period of metabolic adaptation being required. Thus 1 dose of aminophyllin (90 mg/kg) had no effect, but glucose uptake was increased significantly by 45 mg/kg/day for 8 days. (23 refs.)

Psychiatrische und Neurologische Klinik
Universität des Saarlandes
Homburg/Saar, Germany

1717 Lendle, L. Arzneimittelnebenwirkungen in der Kritik der Pharmakologie. [Drug side effects from the point of view of the pharmacologist.] *Medizinische Wochenschrift*, 1962, 104, 61-67.

In a general discussion of the causes, prediction and prevention of side effects due to all types of natural and synthetic drugs, including specifically the phenothiazines, the author distinguishes between true dosage-dependent side effects and allergic reactions, and suggests that the risks of side effects are often overrated. Particular attention is paid to the pharmacological evaluation of the risk of side effects by determination of the spectrum of action, relative specificity, metabolism, biochemical effects and immunological effects of drugs and their combinations on a variety of animal species. Even then final evaluation can only be made on the basis of long clinical experience with sick patients and accurate reporting. (6 refs.)

Pharmakologisches Institut
Universität Göttingen
Göttingen, Germany

1718 Sahli, M. Zur Analytik der Rauwolfia-Alkaloide. [Quantitative determination of the Rauwolfia alkaloids.] *Arzneimittel-Forschung*, 1962, 12, 55-61, 155-61.

Following a review of the chemical structure of the principal Rauwolfia alkaloids, including the quaternary anhydronium bases and the tertiary indol and indolin bases, extraction methods used for their separation are briefly discussed. The spectrophotometric (UV and infrared), colorimetric and fluorometric determination of the individual pure alkaloids, with particular attention to reserpine and its degradation products are reviewed; analytical results on some of the commercial preparations of reserpine are presented. Methods are also described for the determination and characterization of total Rauwolfia alkaloids by means of countercurrent distribution, chromatography on columns, paper or films, and paper electrophoresis. Finally the author's personal experience with the paper chromatography of serpentine, reserpine, reserpine acid, rescinnamine, deserpidine and ajmalin is reported. (138 refs.)

Laboratorium der Interkantonalen
Kontrollstelle für Heilmittel
Bern, Switzerland

1719 Janz, Dieter. Gezielte Therapie der Epilepsien. [Specific treatment in epilepsy.] *Medizinische Welt*, 1962, No. 12, 629-635.

After reviewing the etiology of epileptic attacks and deploring the limited use of anticonvulsive agents in practice, the author points out that the type of treatment should be determined by the type of attack rather than by the etiology. The importance of proper dosage is emphasized, and side effects are grouped into 3 types; hypersensitivity reactions, effects on hematopoiesis, and minor effects varying with the drug and dosage used. Tables are presented listing the chemical composition, dosage used, and price of the anticonvulsive agents on the German market. General suggestions for the control of side effects and management of treatment, the indications and contraindications for the most effective drugs in the various types of epilepsy (on the basis of 3350 cases), and the dosage and side effects of 2 of the most important barbiturates, hydantoins, succinimides and oxazolidines are given. The sulfonamide derivative Ospolot, mentioned briefly, does not seem to be effective in psychomotor epilepsy (61 cases). (10 refs.)

Nervenklinik der Universität Heidelberg
Heidelberg, Germany

1720 Lüth, Paul. Der praktische Arzt und die neuen Medikamente. [The general practitioner and the new drugs.] *Münchener Medizinische Wochenschrift*, 1962, 104, 81-84; 128-131.

In a general discussion of the requirements for critical evaluation of new drugs in general practice (animal experiments, toxicity studies in normal individuals, statistically evaluated placebo studies and pilot studies to evaluate the dependability of patients), presented at the Salzburg Congress of the International Society for Applied Medicine in 1961, the author emphasizes that most of the overwhelming numbers of new drugs are directed at the hospitalized patient and that the problems faced by the individual practitioner are quite different. The need for complete information on the pharmacological properties of new drugs is stressed, with

particular attention being drawn to the confusion in the field of psychopharmacology. (26 refs.)

Kaiserstrasse 8-3/10
Offenbach am Main, Germany

1721 Ulrich, J. Die konservative Therapie der Epilepsie. [Conservative treatment of epilepsy.] Praxis, 1962, 51, 62-67.

In addition to reviewing the psychological aspects of epilepsy and the general guidelines for the management of this disease by proper living, the author classifies the currently used anticonvulsants into 2 groups: those which are effective in all cases except petit mal with 3/second spikes and waves (phenobarbital, diphenylhydantoin, meph-enytoin and primidone), and those which are effective only in this type (trimetha-done, trimethadione, acetazolamide and succinimide); dosages and side effects are listed, and the clinical characteristics of each of these classes of compounds are reviewed in detail. The lack of correlation between etiology and response to specific drugs is pointed out, and suggestions are made as to the best mode of treatment in particular situations. (30 refs.)

Medizinische Klinik des Kantonsspitals
St. Gallen, Switzerland

1722 Stucki, A. Angst, Hemmung, Minderwertigkeitsgefühl. [Anxiety, inhibition and feelings of inferiority.] Praxis, 1962, 51, 148-154.

Following a general discussion of the nature, etiology and function of anxiety and its relationships to inhibition and feelings of inferiority, the author points out that psychotherapy is still the treatment of choice in such conditions. Various ways in which anxiety can be relieved are analyzed. Even though many psychotropic drugs, such as meprobamate, have a superficially beneficial effect on anxiety, they merely mask the underlying condition, destroying the body's alarm signal, often delaying causal therapy. Although tranquil-izers may be necessary temporarily in acute states, the dangers of addiction and

paradoxical effects are emphasized. The negative effects of meprobamate on per-sonality are illustrated by a personal experience. (23 refs.)

Bälliz 64,
Thun, Switzerland.

1723 Hartmann-von Monakow, K. Der heutige Stand der medikamentösen Therapie des Parkinsonsyndroms. [Present status of the drug therapy of the Parkinsonian syndrome.] Praxis, 1962, 51, 30-33.

The indications, clinical response and side effects of a large number of drugs are briefly reviewed. Agents used on the treat-ment of Parkinsonism are divided into alkaloids (tropeins, erthroidin, Rauwolfia), synthetics (aminoesters, phenothiazines, glycerol ethers, aminoethers, propanol derivatives and glutarimides), vitamins (B₆ and B₁₂), hydrazines (MAO inhibitors), and imipramine. Particular attention is devoted to cisternal therapy with Impletol (procaine and caffeine). All these agents, however, are purely symptomatic. (5 refs.)

Dufourstrasse 16
Zürich, Switzerland

1724 Merritt, H. Houston. The neurologi-cal and psychiatric implications of basic studies of the ultrastructure of the nervous system. Bulletin of the New York Academy of Medicine, 1962, 38, 813-816.

Despite the vast conglomeration of know-ledge which has been amassed about the CNS, the following information must be obtained to enable man to comprehend the more elusive aspects of mental and neuro-logical disease: the intimate structure and detailed biochemistry of the neurone, the means by which the cerebellum, brainstem nuclei and basal ganglia influence muscle tone and the mode of interaction between spinal cord, brainstem, thalamus and cerebral cortex. Only comprehensive knowledge of the chemical composition of the neurone and other CNS tissues accompanied by an understanding of the affiliated enzyme systems will explain the selective vulnerability which predis-poses certain cells to react selectively to

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specific infections or toxins. Inherited defects in the basal ganglia may lead to greater vulnerability to certain exogenous toxins, e.g., drug-induced parkinsonism. Numerous degenerative diseases and metabolic disorders await future elucidation before they can be effectively ameliorated. (No refs.)

Department of Neurology
Columbia University College of
Physicians and Surgeons
New York, N. Y.

1725 Inglis, W. Drug company's responsibility. New Zealand Medical Journal, 1962, 61, 562. [Letter]

On behalf of the Geigy Chemical Co., the medical director states that many years of research and investigation preceded the release of imipramine to the public. Treatment of overdoses may be specified only after sufficient data on the subject has been accumulated. At present, the dearth of available data means that treatment must be based solely upon knowledge of the product especially with respect to potential toxicity. Labels which extensively proclaim possible deleterious drug effects can only cause unnecessary consternation on the part of the lay public. The drug company should provide doctors with the complete story of a drug, not an emphasis on side effects. It is further suggested that all potentially dangerous compounds be packaged in the most unattractive form possible. Parents should exercise extreme caution in handling drugs where children are concerned. (No refs.)

[No address]

1726 Cumming, A. Alcoholism. Medical Services Journal (Canada), 1962, 18, 787-794.

Alcoholism, a personality disorder whose chief symptom is chronic compulsive drinking, has roots which are deep in the unconscious. Signs which are suggestive of alcoholism include: the morning drink, severe and remorseful hangovers, sneaking drinks, blackouts, loss of appetite, solitary drinking, concealing liquor, decreased

efficiency, personal problems, lying about alcohol consumption and characteristic personality changes. Alcoholism exists in people who require strong oral gratification, and, while it cannot be cured, it can be controlled. The Canadian army advocates the following treatment regimen for alcoholics suffering from acute withdrawal symptoms: no alcohol, chlorpromazine (50 mg t.i.d.), vitamin B complex (1 cc. i.m. b.i.d.), crystalline insulin (5-10 units 30 minutes before meals) and sodium amytal (3 gr. at bedtime). Membership in Alcoholics Anonymous offers the best opportunity for rehabilitation. (No refs.)

[No address]

1727 Odegard, Ornulv. 3. internasjonale kongress for psykofarmakologi i München 2.-5.IX.1962. [Third International Congress for Psychopharmacology in Munich, 2-5 Sept., 1962.] Nordisk Medicin, 1962, 68, 1457-1459.

The research departments of major drug companies and the leading psychiatric hospitals over the world were well represented at the 3rd International Congress for Psychopharmacology. About 350 delegates attended. The tone of this congress was reserved compared to the optimism exhibited in 1958. The debate between the optimistic New York group with Kline and the critical Maudsley group with Shepherd was both useful and entertaining. Placebo research appears to be declining, and less interest was expressed in the double-blind method as the only method permitted in research. In animal research the tendency is away from Pavlovian methods to behavioral research. Additionally a warning was given against the promiscuous use of minor tranquilizers. (No refs.)

[No address]

1728 Baeyerts, John D. The effect of Librium. New Zealand Medical Journal, 1962, 61, 368-369. [Letter]

Sedatives such as amytal (1/2 to 3/4 grains t.i.d.), aspirin or codeine are as effective as chlordiazepoxide in alleviating primary dysmenorrhea in young women with bright vivacious personalities who are apparently predisposed to dysmenorrhea since they have rather low pain thresholds and are very sensitive to painful stimuli. Any drug which tends to diminish the characteristic conscious or subconscious hyper-reactivity exhibited by these women increases tolerance to pain and obviates distress. It is essential to reassure these patients that no organic anomaly exists, and explain that premenstrual pain is a natural phenomenon which occurs to a varying extent in the majority of young women. (No refs.)

[No address]

1729 Wunderlich, H. Phenothiazinbasen als Spasmolytica. [Phenothiazine bases as spasmolytic agents.] Pharmazie, 1962, 17, 269-276.

A brief historical review of the development of the phenothiazines and the relationship between antihistaminic and CNS activity is followed by a comparison of the pharmacological properties of the phenothiazines in current use and a detailed analysis of the structural components leading to various types of spasmolytic activity. The high degree of potential variability offered by the phenothiazine ring system and the utility of distinguishing between histaminolytic, acetylcholinolytic, nicotinolytic, parkinsonolytic and other types of spasmolytic activity are emphasized. The main structural requirements for spasmolytic agents are a large polarizable group connected to a cationic moiety by means of a short alkyl chain. Particular attention is given to the development of strong quaternary bases which potentiate the activity of the cationic moiety and enhance the spasmolytic properties. The differential effects of various quaternary substituents are compared. Space is also devoted to the carbonyl, carboxyl and carbosulfonyl derivatives of phenothiazine, the spasmolytic properties of which are currently under investigation. By means of such structural modifications, effects on striated

muscle can be obtained which render the compounds valuable in the treatment of extrapyramidal spasticity. (59 refs.)

Westendring 22
Dresden, Germany

1730 Voigt, R. Psychopharmaka. Chemie und Wirkung pflanzlicher und synthetischer psychotroper Verbindungen. [Psychotropic drugs. The chemistry and pharmacology of psychotropic substances, both synthetic and those derived from plants.] Pharmazie, 1962, 17, 317-331.

In an extensive review of those agents with a primary effect on the CNS, as distinguished from alcohol, caffeine, morphine, etc., which have secondary psychotropic effects, the author classifies psychotropic drugs into 2 broad groups: psychotherapeutic and psychotomimetic agents. The former are subdivided into neuroleptics (Rauwolfia derivatives, phenothiazines, azaphenothiazines, thiaxanthenes, diazepins), ataractics (diphenylmethanes, aliphatic alcohols, carbamates), psychotonics (phenylethylamines, amphetamines) and thymoleptics (hydrazines, dibenzazepins). Among the psychotomimetics, mescaline, harmaline, tryptamine derivatives, lysergic acid derivatives and psilocybin are discussed, and some structure-activity relationships are pointed out. (201 refs.)

Pharmazeutisches Institut
Humboldt Universität
Berlin, Germany

1731 Pfeifer, S. Zentrale Analgetica. [Central analgesics.] Pharmazie, 1962, 17, 189-203.

This is an extensive review of the chemistry and pharmacology of the principal types of centrally acting analgesics, with particular reference to structure-activity relationships. A brief historical review of the development of the semi-synthetic morphine derivatives is followed by a detailed analysis of the interrelationships in the morphinan, pethidine, methadon and benzimidazol groups. The principal structural components in an analgesic include a central C or N atom

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with decreased electron density, one or more lipophilic aromatic rings, a cationic group attached to the active center by a C-C chain, and hydrophilic residues. (178 refs.)

Pharmazeutisches Institut
Humboldt Universität
Berlin, Germany

1732 Dundee, John W., & Moore, James. The phenothiazines. *British Journal of Anaesthesiology*, 1962, 34, 247-250.

The phenothiazines, 7 with dimethyl amino propyl side chains, 4 with piperazine side chains and 2 with piperidine side chains are classified in tabular form, replete with information on proprietary names, radicals, average clinical dosages, indications for common clinical usage and frequently reported side effects. No relationship has been observed between analgesic activity and chemical grouping. (46 refs.)

Department of Anaesthetics
The Queen's University of Belfast
Great Britain

1733 Kety, Seymour S. Regional neurochemistry and its application to brain function. *Bulletin of the New York Academy of Medicine*, 1962, 38, 799-812.

Esoteric experimental techniques have enabled scientists to learn a considerable amount about brain function, metabolism and blood supply. The role of catecholamines (such as levarterenol and serotonin) in brain metabolism has been elucidated. Psychoactive drugs like LSD, iproniazid and reserpine have resulted from extensive research. Neurochemistry provides the key to unlock new thresholds of understanding which will in turn provide the basis for significant future achievement. (47 refs.)

Laboratory of Clinical Science
NIMH
Bethesda, Md.

1734 Amark, Curt. 5. Internationella

psykoterapikongressen i Wien, 21.-26. VII.1961. [Fifth International Psychotherapy Congress in Vienna, 21-26 August, 1961.] *Nordisk Medicin*, 1962, 68, 1529-1533.

In the 5th International Psychotherapy Congress in Vienna many talks centered on the relationship between psychotherapy and psychopharmacology. Drugs work on mood but not individual experience. Correct diagnosis is stressed in any event. An ordinary drug can be used by a patient as a defense so that he maintains his neurotic symptom. Also complaints are registered against the preponderance of drug advertising. Finally, group therapy, conjoint family therapy, etc., are mentioned. (No refs.)

[No address]

1735 Shama Rau, T.H., & Mukerji, G. Indigenous drug research. *Probe*, 1962, 1, 205-210.

A number of Indian plant species are discussed, including *Rauwolfia serpentina*, *Nardostachys jatamansi* (jatamansic acid useful in the treatment of epilepsy, hysteria and convulsions) and *Echinops echinatus* (a nerve tonic; a crystalline alkaloid which has been isolated and found to be a smooth muscle relaxant). Two works are cited: "Glossary of Indian Medicinal Plants" by the Council of Scientific and Industrial Research [India] and the Indian Pharmaceutical Codex published by the Central Drug Research Institute, Lucknow, India. The latter volume contains about 190 monographs on Indian drugs. (No refs.)

Central Drug Research Institute
Lucknow, India

1736 Stephen, Elspeth. Carisoprodol. *Developmental Medicine and Child Neurology*, 1962, 4, 80-83.

The value of carisoprodol in infantile cerebral palsy and difficulties in evaluation are discussed. In most cases there is no way of determining the level of the lesion or

lesions in the CNS except by clinical impressions. Emphasis is placed on the report of Denhoff and Holden (1961), in which muscle relaxants were studied in a well controlled trial, i.e., each drug matched with placebo. Behavior and neuromuscular function were studied and these authors concluded that placebo had greater effectiveness in both categories. Further, the need for accurate record keeping concerning palsied children is stressed. (4 refs.)

[No address]

1737 Janssen, Paul A.J. A review of the chemical features associated with strong morphine-like activity. *British Journal of Anaesthesia*, 1962, 34, 260-267.

Chemical data is presented on the common stereoisometric chemical features found among the compounds that are known to display physical morphinelike properties at low dose levels. Emphasis is placed on the potent long acting biocompounds related to the methidone-type as well as to the pethidine-type of compound. As morphinelike molecules look alike chemically, it appears reasonable that there is a common receptor area in the brain, possibly in the thalamic area. (16 refs.)

Research Laboratorium Dr. C. Janssen
Beerse, Belgium

1738 Lindgaerde, Odd. Klassificering af nyere psykofarmaka. [Classification of new psychopharmaca.] *Nordisk Medicin*, 1962, 68, 1432-1433. [Letter]

In reply to Schou [Abstract 1739] the writer states that his purpose in presenting a drug classification was not to institute anything new, but to introduce order into the confusion which has already caused too many misunderstandings in psychopharmacology. The need for agreement in classification is stressed. The writer does not support Schou's contention that a special group should be formed for the imipramine-amitriptyline drug group used in manic depressive psychoses. (3 refs.)

[No address]

1739 Schou, Mogens. Klassificering af nyere psykofarmaka. [Classification of new psychopharmaca.] *Nordisk Medicin*, 1962, 68, 1431-1432. [Letter]

In a criticism of Lingjaerde (1962), the writer took the view that his classification was not new or different, and favored Jacobsen's (1959) WHO report. (9 refs.)

[No address]

1740 McKay, D.N. The toxic substance (thalidomide) prohibition notice, 1962. *New Zealand Medical Journal*, 1962, 61, 474.

Thalidomide was prohibited in Wellington on the 15th of August, 1962, by a proclamation which decreed that the importation, manufacture, sale, possession or use of the toxic substance known as thalidomide was henceforth prohibited by law for a period of precisely 1 year. (No refs.)

Ministry of Health
Wellington, New Zealand

1741 Schmidt, Richard Penrose. Epilepsy in adults. In: Conn, Howard F. [Ed.] *Current Therapy*. Philadelphia: W.B. Saunders, 1962. Pp. 508-511.

The following types of therapy are advocated to ameliorate epilepsy in adults: grand mal and focal cortical seizures respond to diphenylhydantoin or primidone, psychomotor attacks also respond to these drugs, plus methsuximide where indicated. Petit mal seizures may be alleviated with trimethadione, phenobarbital, paramethadione or methsuximide while unclassified seizures (myoclonic attacks, drop seizures, minor seizures of uncertain origin) respond more readily to primidone than to diphenylhydantoin. New compounds such as ethosuximide are effective in petit mal and psychomotor seizures. Severe refractory epilepsy may respond to drugs like methyl-phenyl-ethyl hydantoin, phenacemide, mephobarbital or acetazolamide. Toxic effects are similar and generally encompass excessive drowsiness, unsteady gait, visual blurring with nystagmus and, occasionally, granulocytopenia or

agranulocytosis. Surgical intervention may sometimes be indicated. Status epilepticus frequently responds to paraldehyde, amobarbital or tribromethanol. Emotional rehabilitation is essential to patient wellbeing. (No refs.)

[No address]

1742 Regan, Peter F. Psychoses: Delirium. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W.B. Saunders, 1962. Pp. 552-555.

Treatment of the initial phase of delirious reactions involves diminution of all excitatory external stimuli. During the 2nd phase, mounting anxiety and insecurity necessitate precautions against suicide, mandatory obviation of all excitatory stimuli must be enforced, hypnotics may be used to induce sleep and tranquilizers such as chlorpromazine (25 mg q.i.d., i.m.) may be found advantageous. The 3rd phase of delusion is characterized by complete loss of contact with reality, delusions, hallucinations and serious disorientation and the patient must be prevented from committing suicide. Agitation may be controlled by administration of barbiturates or phenothiazines, particularly chlorpromazine, with dosage regulated according to need. The patient must receive adequate nourishment with careful control of body processes. Special treatment regimens are advocated in instances of deliria occurring in drug withdrawal, toxic and metabolic deliria, deliria associated with drug administration, postoperative deliria and deliria associated with injury to the CNS. (No refs.)

University of Florida
Gainesville, Fla.

1743 Marks, John. Current views on psychotropic drugs. New Zealand Medical Journal, 1962, 61, 391-397.

Tranquilizers are classified primarily on the basis of their pharmacological and clinical properties rather than by their chemical constituents. A 2nd method of chemical classification divides the compounds into 4 main groups: pheno-

thiazine derivatives and analogues, reserpine and its derivatives, propanediol derivatives and diphenylmethane derivatives. All are presented in tabular form with accompanying trade names. Selection of the drug of choice for a particular patient is based primarily upon the mode of drug action, as these compounds act at cortical and midbrain levels predominantly on centers concerned with emotional responses. With respect to biochemical mechanisms of action, the catecholamines appear to affect mood by precipitating the release of bound amines, preventing free amine breakdown, obviating transport across membranes and releasing amines while preventing their resultant breakdown. Imipramine and amitriptyline antagonize the effects of reserpine-type compounds while the tranquilizers do not. All known compounds alleviate symptoms without altering the underlying psychopathology. Eventually compounds will be developed which are capable of effecting valid cures. At present, the psychoactive drugs constitute a rather sizeable percentage of the drugs currently available to the public. (No refs.)

[No address]

1744 Steinhilber, Richard M. Psychoses: Schizophrenia. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W.B. Saunders, 1962. Pp. 541-544.

Schizophrenia is currently treated with various psychotropic drugs (Rauwolfia derivatives, methaminodiazepoxide, chlorpromazine, trifluoperazine, prochlorperazine, perphenazine, mepazine, etc.), insulin shock therapy, ECT, psychosurgery, hypnosis and psychotherapy. All of these adjuncts are utilized as indicated on an individual basis to transform the acutely or chronically disturbed patient into a functioning member of society. (No refs.)

Mayo Clinic
Rochester, Minn.

1745 Chao, Dora. Epilepsy in children. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W.B. Saunders, 1962. Pp. 511-516.

A single seizure in children does not necessarily connote the inchoation of epilepsy per se. Therapy of such incidents is based upon amelioration of the underlying lesion rather than institution of continuous anticonvulsant therapy. Febrile convulsions and status epilepticus should be dealt with immediately, and every effort made to forestall future seizures with anticonvulsants, particularly diphenylhydantoin. Epilepsy of cerebral origin is generally divisible into petit mal seizures which respond to trimethadione, acetazolamide, phenisuximide, chloroquine and ethosuximide, the petit mal triad (absence of myoclonic and akinetic attacks) which reacts favorably to methsuximide, dexedrine and benzedrine, and seizures other than petit mal that respond to the hydantoins, barbiturates, primidone, amino-glutethimide, methsuximide and meprobamate. Diet and surgical treatment are useful where indicated. General rules for the management of epilepsy are presented, and relevant data on drugs now used to control childhood epilepsy is presented in tabular form. (1 ref.)

[No address]

1746 Mann, Warren A. Alcoholism. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W. B. Saunders, 1962. Pp. 488-490.

The treatment regimen for alcoholism relies heavily upon methaminodiazepoxide, with dosage adjusted to accommodate individual requirements. Simple intoxication may progress from mild to moderate and even severe stages, with respiratory depression (requiring nikethamide or methylphenidylacetate) and circulatory collapse. Withdrawal symptoms such as psychomotor agitation, convulsions, insomnia, acute hallucinosis and Korsakoff psychosis all respond to a variable degree to administration of methaminodiazepoxide. Treatment for the chronic phase is designed to prevent future exacerbations. Chronic alcoholism carries with it the risk of deleterious somatic side effects such as peripheral neuritis, gastritis, gastrointestinal hemorrhage, respiratory and cardiovascular complications. Alcoholics should receive chemical barriers to curtail drinking, such as tetraethylthiuram, and

psychological bolsters like Alcoholics Anonymous in addition to familial understanding and cooperation. (No refs.)

[No address]

1747 Payne, Charles E. The out-patient treatment of depression. American Practitioner, 1962, 13, 643-648.

Depression is manifested by early awakening insomnia, anorexia, crying, poor concentration, impaired thinking ability, and a host of complaints which often mimic somatic illness. Development of the antidepressant drugs such as imipramine and chlorthalidoxepoxide have enabled psychiatrists to treat depression in ambulatory patients. Elucidation is offered on the hazards of suicide, prognosis, diagnosis and treatment of depression per se. A hypothetical case is presented to illustrate current modes of therapeutic management. Emphasis is placed on patient awareness of possible drug-induced side effects, with precise instructions on what to do in the event of an emergency. Thorough explanation should precede any therapy with psychoactive drugs. (1 ref.)

[No address]

1748 Regan, Peter F. Psychoses: Manic-depressive reactions. In: Conn, Howard F. [Ed.] Current Therapy. Philadelphia: W. B. Saunders, 1962. Pp. 546-551.

The treatment of the depressive phase of manic-depressive psychosis includes protection of the patient by initially determining suicide potential, followed by stabilization by means of regular office therapy, home or hospital treatment, development of an activity program encompassing patient mobilization, occupational therapy, expansion of the scope of interests and increasing satisfaction obtained from daily pursuits, in conjunction with a program of psychotherapy. Depression responds to meprobamate, ECT and the antidepressant drugs (imipramine, iproniazid and nialamide). Manic excitement responds to similar therapy, with considerable emphasis on protecting

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the patient from bodily harm. Activity, psychotherapy, ECT and the phenothiazines are all efficacious in ameliorating mania. Chlorpromazine, promazine, and trifluoperazine are particularly useful as adjunctive therapy, despite the fairly serious side effects which may be manifested. (No refs.)

University of Florida
Gainesville, Fla.

1749 Naess, Knut. Medikamenter og blod-dyskrasier. [Drugs and blood dyscrasias.] *Nordisk Medicin*, 1962, 67, 58-60.

In a general discussion centering largely on the work done by the Study Group on Blood Dyscrasias of the AMA Council on Drugs, chlorpromazine-induced and imipramine-induced blood dyscrasias (leukopenia) are noted. (No refs.)

Sturegatan 16
Stockholm, Sweden

1750 *Journal of the American Medical Association*. Glue-sniffing. *Journal of the American Medical Association*, 1962, 184, 123. [Editorial]

Plastic cements and airplane glue are currently inhaled by teenagers to induce euphoria and exhilaration. Habitual inhalation may lead to intoxication, disorientation and coma. Detrimental effects on the senses derived from vapors of glue, paint thinners, lacquers, enamels and marking pencils are apparently due to the organic solvents within these products. Glue-sniffing may also produce various deleterious effects on different organ systems. Apparently, glue-sniffing is highly correlated with delinquency, and frequently is the precipitating factor which brings delinquents before the juvenile court. In Denver alone, arrests for glue-sniffing increased from 30 to 134 in 1 year. Further investigations are contemplated on the physical, social and emotional implications of noxious vapor inhalation. (1 ref.)

Journal of the American Medical Association
535 N. Dearborn Street
Chicago 10, Ill.

1751 Huvanandana, Malai. The centre for treatment and rehabilitation of opium addicts, Rangsit, Thailand. *Bulletin on Narcotics*, 1962, 14, 1-6.

Opium smoking was made illegal in Thailand on July 1, 1959. The sanatorium at Tambol Rangsit, Ampur Tanyaburi, Patumthani province, Thailand is described. The center, 43 kilometers from Bangkok, consists of 3 sanatoria, 5 convalescent houses, 5 dining-rooms and kitchens, a police station, 134 lodging apartments for officials and miscellaneous work shops. Data are presented for 1959, i.e., the number of admissions, readmissions, deaths, escapes, etc. (No refs.)

Department of Public Welfare of Thailand
Bangkok, Thailand

1752 *Clinical Medicine*. Insulin coma therapy in psychiatry. *Clinical Medicine*, 1962, 69, 2013. [Editorial].

Insulin coma therapy was administered to 2033 schizophrenic patients with the result that full recovery was observed in 69%, much improvement in 9%, improvement in 5% and no improvement in 17%. Insulin coma therapy combined with ECT at the deep coma level was administered to 189 out of 346 who failed to react to insulin shock, and 168 patients exhibited full recovery. A combination of deep insulin coma and ECT has frequently salvaged many patients who would otherwise be permanently hospitalized. (No refs.)

[No address]

1753 Meyler, L. Bloedveranderingen door geneesmiddelen. [Drug-induced changes in the blood picture.] *Geneeskundige Gids*, 1962, 40, 87-93.

After distinguishing between changes in the blood picture due to drug intoxication or overdosage and those due to allergy or idiosyncrasy, the author reviewed the possible etiology and diagnosis of thrombocytopenia, pancytopenia, agranulocytosis and hemolytic anemia, giving examples in each case of drugs which have caused these

conditions. Among the psychotropic drugs listed which produce thrombocytopenia are: apronalide, aminopyrine, chlorpromazine, imipramine, hydantoin and antihistamines which produce agranulocytosis, and phenacetin which may produce hemolytic anemia. (9 refs.).

[No address]

1754 Serra, Carlo. The enzymic activation of the electroencephalogram. *Acta Neurologica Scandinavica*, 1962, 38, 64-65.

Modifications of EEG recordings resulting from altered enzymatic activity in glucose metabolism include the following: i.v. cocarboxylase induces decreased electrocortical activity which migrates from temporal to anterior cortical regions, ATP administered i.v. to normal subjects produces photic driving patterns in response to intermittent photic stimulation which resemble patterns elicited from neurotics and interference with cytochrome systems produces EEG patterns which vary according to basic physiological conditions (e.g., congenital heart disease). Preliminary observations with malononitrile have corroborated the influence of cyanide on brain cytochrome systems, and consistent EEG changes observed as photic driving patterns have confirmed the importance of lipoic acid in the oxidative decarboxylation of pyruvic acid. These substances condition the complex physicochemical changes which are responsible at the cellular level for inducing continuous variations in electrical potential. (13 refs.).

Neurophysiological Department
Centro Traumatologico Ortopedico, Inail
Naples, Italy

1755 Glatt, M. M. The abuse of barbiturates in the United Kingdom. *Bulletin on Narcotics*, 1962, 14, 19-37.

The historical background of the use of hypnotics in the United Kingdom, dating from the introduction of chloral hydrate in 1869, is reviewed with emphasis on the controversial aspects of use and abuse. Data is presented on barbiturate consump-

tion, acute barbiturate poisoning (suicides and accidental deaths, and attempted suicides), barbiturate habituation, addiction and chronic intoxication, and information on alcohol. The need for education, psychotherapy and the development of less toxic drugs is stressed. The new nonbarbiturate hypnotics, while fairly satisfactory and probably less toxic and less habit forming, are not free from dangers and also seem slightly less effective than the barbiturates. (16 refs.).

[No address]

1756 Arlen, Monroe S. Emergency assessment and management of the potential suicidal patient. *Clinical Medicine*, 1962, 69, 1101-1118.

A comprehensive treatise on depression includes various analytically oriented definitions and theories of etiology, characteristics of depression, the relationship between grief and depression, and basic diagnostic categories (reactive depression, psychotic depressions, mania and involuntional psychotic reactions). Suicide risk may be assessed on the basis of the following criteria: depth of depression, severity of despair, communication of suicidal intent, loss of contact with reality, previous suicidal attempts, suicide notes, traumatic anniversary reactions and various other indications. Indications and contraindications for hospitalization are presented, along with the need for a positive approach and avoidance of emotional blackmail. The physician should offer some support in making difficult but essential decisions. Elderly patients must be made to feel wanted. Several common misconceptions regarding suicide are dispelled in question and answer form. Drugs are of little value if results are mandatory in less than 12 hours. Anxiety, tension, irritability and restlessness may be ameliorated by meprobamate or chlordiazepoxide. Amphetamines may be helpful, and new antidepressants such as MAO inhibitors and imipramine may be efficacious over a period of several weeks. Sedatives and phenothiazines should be avoided, as they tend to deepen depression. (3 refs.).

Lawton, Okla.

1757 Córdova Castro, Armando. Aspectos psiquiátricos del asma bronquial. [The psychiatric aspects of bronchial asthma.] Revista Cubana de Medicina, 1962, 1, 33-38.

In a discussion of the psychogenic factors involved in asthma, the utility of chlorpromazine in small doses, meprobamate, reserpine, imipramine and methylphenidate, as well as Gorbadei's (1960) novocaine therapy are elucidated. (15 refs.).

Psiquiatra del Hospital Cmte. M. Fajardo
Havana, Cuba

1758 Liberson, W. T. Electroencephalography. American Journal of Psychiatry. 1962, 119, 607-611.

New developments on the use of electroencephalography in studying sleep, mental activity, evoked potentials, rheoencephalography (recording of intracerebral impedance contributing to the study of vascular lesions) and psychopharmacology. Comparison of the effect of chlorpromazine, imipramine and placebo suggests that EEG frequency analysis provides quantification of neurophysiological changes with psychotropic drugs for psychiatric research. Extensive studies were also performed with chlordiazepoxide. Considerable work has been done on determining abnormal EEG's in mental patients, free of any history of organic or epileptic disorder. Schizophrenic patients with abnormal EEG records showed a higher sensitivity to treatment, both from the clinical and EEG point of view.

V.A. Hospital
Hines, Ill.

1759 Ayd, Frank J. The impact of psychopharmaceuticals on psychiatric units in general hospitals. American Journal of Public Health, 1962, 52, 13-15.

Since 1955, the Franklin Square Hospital in Baltimore, a general hospital with no psychiatric division, has admitted over 1,000 psychiatric patients with acute brain syndrome, alcoholism, psychoneurotic dis-

orders, schizophrenic reactions, manic-depressive reactions, etc.) on the medical service and treated them with psychotherapy, drug therapy, sleep therapy, ECT and psychosurgery, for an average hospital stay of 14 days. The current demand for psychiatric treatment in general hospitals far exceeds the facilities offered by the slightly more than 20% of our general hospitals which now accept the emotionally and mentally ill. Such facilities should multiply rapidly in the next few years due to greater improvement in psychoactive drugs and increased psychiatric acumen in utilizing these drugs, as well as increased coverage for psychiatric illnesses by commercial health insurance programs such as Blue Cross. Psychoactive drugs have reduced the number of institutionalized mental patients by more than 23,000 since 1955. The advent of the psychopharmaceuticals has enabled numerous general practitioners to successfully treat psychiatrically ill patients.

Franklin Square Hospital
Baltimore, Md.

1760 Arnold, O. H., Hift, St., & Hoff, H. The role of psychotropic drugs in current psychiatric therapy. Comprehensive Psychiatry, 1962, 3, 330-342.

Five groups of psychotropic drugs are discussed, particularly with regard to clinical effects. The following properties of neuroleptics (reserpine, harmaline, benzoquinolizines, phenothiazines, etc.) are reviewed including neurophysiologic-anatomic aspects, therapeutic applications and side effects. Tranquilizers mentioned included carbamate, bicyclic compounds and benzodiazepine, while antidepressants included imipramine, chlor-imipramine and amitriptyline. Stimulants included weckamine, oxazine derivatives, methylphenidates and hydrazides. Mescaline, LSD, psilocybin and dimethyltryptamine are noted as typical psychotomimetics. (35 refs.)

Psychiatrisch-Neurologische Klinik
Universität Wien
Vienna, Austria

1761 Linke, H. Kritik der Therapie: Nebenwirkungen und Gefahren der Anwendung psychotroper und schmerzstillender Pharmaka. [Criticism of therapy: side effects and dangers in the use of psychotropic and analgesic drugs.] Pharmazie, 1962, 17, 380-393.

In a general review of the principal mental and physical side effects of the analgesics, neuroleptics, tranquilizers, thymoleptics and psychostimulants, the dangers of ambulatory therapy are emphasized, and particular attention is given to the problem of habituation and addiction to analgesic drugs following their prolonged use. The causes for the increasing use of analgesics and tranquilizers are discussed and regulatory measures are suggested, with special reference to the situation in East Germany. (132 refs.)

Medizinische Klinik
Medizinische Akademie Magdeburg
Magdeburg, Germany

1762 Silver, Henry K., & Garell, Dale. Metabolic defects associated with mental retardation. American Journal of Diseases of Children, 1962, 104, 401-418.

A discussion of the metabolic defects associated with mental retardation includes a tabular presentation of numerous metabolic defects with salient clinical features, genetics, urinalysis, biochemical studies and treatment for each disorder. While the exact incidence of mental retardation due to specific metabolic defects is not known, estimations obtained from studies of over 2,000 patients (Yannet 1956) are: 40% with no demonstrable pathology, 16.7% with mongolism, 45% with congenital CNS anomalies, 16.7% with anomalies due to destructive processes occurring in the perinatal period, and 21.6% with inborn errors of metabolism. Diseases discussed at length include: galactosemia, maple sugar urine disease and Wilson's disease. Diseases outlined in tabular form include: arginosuccinuria, aciduria, citrullinuria, cystathioninuria, Hartnup disease, hyperglycinemia, Joseph's disease, Oasthouse disease, phenylketonuria, proline metabolic defect, sex-linked microcephaly and spastic

diplegia, fructose intolerance, idiopathic hypoglycemia (leucine-induced), sucroseria, gargoylism, Gaucher's disease, etc. Understanding of the pathogenesis of mental retardation is contingent upon the acquisition of greater knowledge of the enzyme systems involved and their biogenetics. (114 refs.)

Department of Pediatrics
University of Colorado Medical Center
Denver 20, Colo.

1763 Way, E. Leong, & Adler, T. K. The biological disposition of morphine and its surrogates. Geneva: World Health Organization, 1962, 1-117.

This study on the biology of morphine was originally published in 4 installments in the Bulletin of the World Health Organization (1961-1962). The first 3 parts, which deal successively with morphine, the partially synthetic derivatives of morphine and the wholly synthetic substances with morphine like action, are presented in the form of individual monographs. The morphine and morphinemimetic compounds, by class, are: naturally occurring opium alkaloids, partially synthetic derivatives of morphine, synthetic compounds - morphinans, methidones, phenilpiperidines and miscellaneous (ethoheptazine and phenazocine). The 4th part is devoted to general considerations on this group of drugs as a whole. Absorption, distribution, biotransformation (N-demethylation, O-demethylation, conjugation and hydrolysis) and the excretion of each compound, as well as techniques of evaluation are detailed. (272 refs.).

Department of Pharmacology
University of California Medical Center
San Francisco, Calif.

1764 Bundock, J.B. Canada's new controls of the barbiturates and the amphetamines. Medical Services Journal, Canada, 1962, 18, 464-465. [Editorial]

New Canadian legislation has made trafficking in narcotics or possession for the purpose of trafficking a special offence with appropriate penalties, as well as providing for more effective legal control over the

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importation, manufacture and distribution of these drugs in order to limit their legal use to exclusively medical purposes. The new act is administered by the Narcotic Control Division of the Department of National Health and Welfare, whose staff has considerable experience in enforcing laws pertaining to narcotics. Physicians should always be cognizant of potential misuse and addiction when prescribing controlled drugs. Only limited quantities of such drugs should be prescribed at a given time. The new law also endeavors to establish better control over "goofballs" and pep pills" now in circulation. (No refs.).

[No address]

1765 WHO Technical Report Series (1962), No. 229. World Health Organization Expert Committee on Addiction-producing Drugs: Twelfth report. Bulletin on Narcotics, 1962, 14, 42-43.

Discussion of the following topics comprised the 12th session of the Expert Committee on Addiction-producing Drugs of WHO: use and abuse of khat in East Africa and Arabia with full elucidation of the chemical and pharmacological properties of khat's active principles; the present disconcerting increase in the illicit production and traffic in heroin; an increase in codeine consumption resulting in all probability from the introduction of new proprietary analgesic preparations; the need for new legislation dealing with rehabilitation which aims at reducing the possibility of relapse, which must of course be preceded by successful drug withdrawal, the establishment of treatment and rehabilitation facilities to promote rehabilitation and the development of tests employing the dog and rat to detect addiction-liability. Research is currently being designed to encompass the basic mechanisms and epidemiology of addiction. (5 refs.).

WHO
Geneva, Switzerland

1766 Mol, W. Softenon en peromelle. [Softenon and peromelia.] Geneeskundige Gids, 1962, 40, 219-222.

Following a brief description, with X-ray photographs, of a 2.5 month-old child with multiple congenital obvious deformities, whose mother took thalidomide (Softenon) in early pregnancy, the influence of such deformities in the Netherlands is discussed. Brief abstracts of 17 articles taken from the literature (mostly British) are also presented. (17 refs.).

Groningen, The Netherlands

1767 Offenkrantz, William. Depression and suicide in general medical practice. American Practitioner, 1962, 13, 427-430.

Depression is predicated upon guilt, grief or shame, and a combination of psychotherapy coupled with mood-elevating drugs may result in significant amelioration of depressive symptoms in the hands of a competent physician. The etiology of depression is based primarily on somatic, psychic or a combination of somatic and psychic factors. Biochemically, serotonin and levarterenol may play significant roles in the complex regulation of affective states. Physical symptoms of depression include fatigue, insomnia, impotence, anorexia, constipation and true hypochondriasis. The omnipresent danger of suicide must always be considered in dealing with depressed patients, and restorative psychotherapy should always explore the patient's current life situation and psychological equilibrium with an eye to eliminating any such disastrous desire. (15 refs.)

University of Chicago School of
Medicine
Chicago, Ill.

1768 British Medical Journal. Powerful analgesics. British Medical Journal, 1962, No. 5325, 241-242. [Editorial]

The principal powerful analgesics fall into 3 chemical families typified by morphine, methadone and pethidine, all of which are antagonized by nalorphine, an analgesic structurally related to morphine. All of these have fundamentally similar modes of action and are readily

able to cause addiction. Some nonaddictive analgesic derivatives are available, but their efficacy is limited to relieving mild or moderate pain. Optimal effects are obtained most readily by s.c. administration of morphine and its analogues. All of these analgesics depress respiration, but a combination of pethidine and levallorphan produces maximal analgesia with minimal respiratory depression. Several morphinelike drugs have become established antitussive agents. Decreased drowsiness may be obtained with levorphanol, methadone or pethidine rather than morphine. When analgesic efficacy is paramount, however, morphine is invariably the drug of choice. Chemistry, dosage, and other relevant information on various morphine analogues is presented in tabular form. (18 refs.)

British Medical Association
Tavistock Square
London W.C. 1, Great Britain

1769 Refshauge, W.D. Phenmetrazine and trifluoperazine. Medical Journal of Australia, 1962, No. 2, 58. [Letter]

Trifluoperazine, a pharmaceutical benefit, and phenmetrazine are contraindicated during pregnancy due to possible incipient teratogenicity. Trifluoperazine is not likely to be utilized by pregnant women to any extent, so it will not be removed from the list of drug benefits. Information which has been circulated to doctors in Canada by the Department of National Health and Welfare corroborates the extensive deleterious effects which may accrue from administration of trifluoperazine and phenmetrazine to pregnant women. Phenmetrazine produced extensive fetal diaphragmatic hernias, while trifluoperazine resulted in quadrilateral phocomelia and various other congenital deformities. (No refs.)

[No address]

1770 Winick, Charles. Maturing out of narcotic addiction. Bulletin on Narcotics, 1962, 14, 1-7.

Data for this study consists of the age and length of addiction of addicts in the files of the Federal Bureau of Narcotics who were originally reported during 1955 but not reported again by the end of 1960. There were 5,553 men and 1,681 women in this sample. Although the age range was from 18 to 76 years, a substantial concentration of addicts became inactive in their thirties. Various causes of drug discontinuance were speculated upon, e.g., whether the process is one of maturing out, as a reflection of the addict's life cycle, or as a reflection of the number of years that the addiction process per se continues. Further study of drug discontinuance should yield valuable information for the treatment and control of addiction. (12 refs.)

New York City Council
Narcotics Addiction Research Project
New York, N. Y.

1771 Endicott, Noble A. The problem of controls in the evaluation of psychotherapy. Comprehensive Psychiatry, 1962, 3, 37-46.

In evaluation of psychotherapy the problem of controls is one of the most troublesome. Several studies which demonstrate the necessity of including controls are reviewed as well as the methodologic difficulties which complicate the utilization of controls in psychotherapy outcome studies. Evaluation tests listed include: Thematic Apperception, Bell Adjustment Inventory, the Rorschach and Kent-Rosanoff Free Association. Psychotherapy given with and without a placebo has also been successfully used for assessment of results. Finally, a general discussion of probable solutions to the problem is presented. (42 refs.)

Albert Einstein College of Medicine
Jacobi Hospital
New York, N. Y.

1772 Barbeau, André. Etudes récentes sur les catécholamines. [Recent studies

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on catecholamines.] Union Médicale du Canada, 1962, 92, 42-51.

After reviewing various adrenal dysfunctions and catecholamine metabolism, the role of catecholamines in extrapyramidal disorders and mental conditions was elucidated. The advent of LSD, the mechanism of o-methylation, factors relating to epinephrine, adrenochrome, adrenolutin, taraxein, serotonin and ceruloplasmin, as well as the clinical use of phenothiazines, reserpine and antidepressants are noted. (119 refs.)

Section of Neurologie
Université de Montréal
Montréal, Quebec
Canada

1773 Taussig, Helen B. Thalidomide — a lesson in remote effects of drugs. American Journal of Diseases of Children, 1962, 104, 111-113. [Editorial]

Thalidomide ingested by 50 pregnant women between the 30th and 60th day after the last menstrual period invariably produced phocomelia in the infant. Accurate records from Lenz's study provide documentary proof that even a single dose of thalidomide can produce phocomelia. By August 1962, 3,500 thalidomide damaged infants will have been born in Germany and several hundred will also have been born in Great Britain. Definitive teratogenicity must be corroborated by extensive animal experimentation with thalidomide, but the welter of circumstantial evidence is damning. (No refs.)

Department of Pediatrics
Johns Hopkins Hospital
Baltimore, Md.

1774 Doshay, Lewis J., & Boshes, Louis D. Recent advances in the management of Parkinson patients. Current Medical Digest, 1962, 23, 53-62.

The aims of the National Parkinson Foundation and the Parkinson's Disease Foundation, in relation to the increasing

incidence of Parkinson's disease are reviewed. Physical therapy, neurosurgery, etc. are detailed. The drugs of current utility are: trihexyphenidyl, cycrimine, procyclidine, benztropine, orphenadrine, chlorphenoxamine, ethopropazine, diphenhydramine, scopolamine and dexamphetamine. (16 refs.)

935 Park Avenue
New York, N.Y.

1775 Kurland, Albert A. The clinical application of psychotherapeutic drugs. Bulletin of the School of Medicine of the University of Maryland, 1962, 47, 45-52.

Psychoactive drugs serve 4 major purposes in clinical psychiatry: therapeutic elimination or modification of psychopathological symptoms, transference of latent drug-induced mental phenomena into manifest phenomena by means of narcodiagnostic techniques, inducing psychotic states for experimental psychopathology and determining drug impact on the normal subject in order to interpret therapeutic effects. One clinical psychologist administered chlorpromazine, meprobamate, reserpine, iproniazid, phenobarbital, dexamphetamine and placebos to himself to determine his subjective interpretation of the resultant effects. Responses varied, even with repetition of the same drug. The major tranquilizers which produce antidelusional and antihallucinatory effects plus sedation include the phenothiazines (chlorpromazine, promazine, trifluoperazine and perphenazine) and the rauwolfia alkaloids (reserpine, rescinnamine, and deserpidine). Certain target symptoms are ameliorated by these drugs, but the underlying psychopathology remains unaltered. Treatment of minor emotional disorders accompanied by anxiety or apprehensive coloration entails use of the minor tranquilizers, such as meprobamate and chlordiazepoxide. Nonbarbiturate sedatives and hypnotics include glutethimide, ethchlorvynol and chlorpromazine. The antidepressant drugs are indicated whenever suicide is not immediately imminent, and drugs like imipramine, isocarboxazid and nialamide appear efficacious antidepress-

ants. Of the depressions which are amenable to drug therapy, about 60-75% of those so treated exhibit a good response. Serious drug-induced side effects run the gamut from agranulocytosis and liver atrophy to dizziness and nausea. Multidisciplinary cooperation insures a productive future for the field of psychopharmacology. (6 refs.)

[No address]

1776 Foltz, Louis M. Critical evaluation of tranquilizers. *Journal of the Kentucky State Medical Association*, 1962, 60, 33-738.

The difficulty in evaluation of tranquilizer efficacy is reviewed. Contributing factors include inadequate and conflicting results of tranquilizer studies, placebo effectiveness, and the lower cost of barbiturates, the effects of which are frequently comparable to those of tranquilizers. Seven difficulties of tranquilizer administration are outlined, e.g., patients develop underlying problems and personality disorders when tranquilizers are administered over a long period of time. Various studies are cited and a compendium of drug effects and placebo effects is presented in tabular form. Relief of symptoms produced by tranquilizers tends to obviate the patient's need to ascertain the real causative factors underlying his disorder. Tranquilizers create a false sense of security in the patient and the physician, and some of these compounds are habit forming and addictive. It is imperative that investigators conduct placebo control studies of new drugs to determine their efficacy. Recent studies have shown that placebos have remarkable potency. A study by Gruber revealed that a double dose of placebo is almost twice as good as a single dose in producing a night's sleep. In many studies, placebos have produced more effective results than the active drugs. Widely divergent results have been obtained when meprobamate was compared with amobarbital or phenobarbital in well controlled trials. Thus far, meprobamate has not exhibited any distinct advantage over adequate doses of barbiturates, either as a hypnotic or as a sedative for the relief of neurotic anxiety or tension. Studies

on chlordiazepoxide, prochlorperazine and benactyzine have also been conspicuously lacking in adequate controls. Depression responds well to trifluoperazine. (10 refs.)

[No address]

1777 Ginsburg, Marshall. The treatment of the problem drinker in an overseas theatre by the general medical officer. *Military Medicine*, 1962, 127, 416-422.

Alcoholism has always constituted a serious problem for the military services, particularly in an overseas theatre with attendant stressful conditions. The U.S. Armed Forces have generally consigned treatment of the problem drinker to the psychiatrist and other specialized personnel. A medical regimen is far more efficacious, however, and is predicated upon treatment of coexisting physical disorders frequently associated with chronic alcoholism, as well as vitamins, dietary regulation and tranquilizers like chlordiazepoxide or chlorpromazine. Disulfiram maintenance therapy represents one of the most significant advances in the medical treatment of the problem drinker, but should only be utilized by a physician who is thoroughly familiar with its indications and contraindications. With respect to the therapeutic aspects of the doctor-patient relationship, the physician's acceptance of the patient as a man with a problem deserving medical attention, in place of the moral condemnation he has come to expect, greatly enhances the patient's self esteem. Psychiatric consultations should be obtained wherever possible. Proper management of follow-up studies are essential. The physician must respect the patient's sensitive and exaggerated pride, permitting him to use whatever devices he requires to continue seeking treatment, while simultaneously expecting the patient to assume a considerable degree of personal responsibility for his participation in the treatment program with absolute abstinence as his goal. (34 refs.)

Department of Psychiatry
Cincinnati General Hospital
Cincinnati 29, Ohio

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1778 LaVerne, Albert A. [Editor]
Compendium of neuropsychopharmacology.
Psychotomimetic drugs. Journal of
Neuropsychiatry, 1962, 4, 63-67.

Perusal of numerous current references has yielded considerable information about psychotomimetic drugs like LSD, mescaline, piperidyl benzilate and phen-cyclidine. These compounds have been fully elucidated in chart form, offering generic and trade names, type and action, indications for use, therapeutic rating, side effects, contraindications and cautions, recommended dosage and references under the auspices of the compendium of neuropsychopharmacology. The format of the compendium is also outlined. (22 refs.)

[No address]

1779 LaVerne, Albert A. [Editor]
Compendium of neuropsychopharmacology.
Preparations used in convulsive and other biological therapies. Journal of Neuro-psychiatry, 1962, 3, 399-409.

As a portion of the compendium of neuropsychopharmacology, the following information is presented in tabular form concerning psychopharmacological preparations utilized in convulsive and other biological therapies: generic or trade name, type and action, indications for use, therapeutic rating (effectiveness and toxicity), side effects, contraindications and cautions, recommended dosage and references. Compounds so elucidated include insulin, glucagon, pentamethylentetrazol, succinylcholine, hexafluorodiethyl ether, tetramethylsuccinimide and CO₂. Explanations for all charts are provided. (49 refs.)

[No address]

1780 Evans, Wayne O. The synergism of autonomic drugs on opiate or opiate-induced analgesia: a discussion of its potential utility. Military Medicine, 1962, 127, 1000-1003.

The autonomically active agents which potentiate the analgetic activity of opiates include parasympathomimetic agents

(neostigmine and physostigmine), parasympatholytic drugs (atropine and scopolamine), sympathomimetic agents (dexamphetamine and methamphetamine), sympatholytic drugs (chlorpromazine and dibenzylamine) and drugs of the tryptamine and tryptophane type. Of the opiate potentiators, dexamphetamine offers the greatest practical utility because of its ability to counteract the side effects of morphine action which tend to increase the danger of shock and produce physical and mental depression. In dogs, rats, mice, healthy people and patients, the addition of dexamphetamine to an opiate will increase its analgetic potency from 60 to 100%. At the same time the addition of dexamphetamine helps to normalize the opiate side effects of respiratory depression, lowered oxygen consumption, hypotension, mental depression, constipation and nausea. Apparently, dexamphetamine potentiated opiate analgesia could be of great use as a combat military analgesic and its potential should be extensively investigated. (28 refs.)

Psychology Division
U.S. Army Medical Research Laboratory
Fort Knox, Ky.

1781 Editorial. Advances in drug research. Clinical testing with thalidomide. South Dakota Journal of Medicine and Pharmacy, 1962, 15, 342-343. [Editorial]

The medical director of the Wm. S. Merrell Company emphasizes the fact that all clinical work with thalidomide was terminating further investigation when reports of drug teratogenicity appeared in Europe. When the 1st report of adverse reactions was received from Germany in November, 1961, clinical investigators were immediately notified that thalidomide was contraindicated for women of childbearing age. In March, 1962, the thalidomide clinical testing program was terminated and participating physicians were requested to return their remaining supplies of thalidomide. At the present time, little if any thalidomide remains in the hands of the clinical investigators and their affiliated institutions. The FDA has been provided with the names of testing physicians, and in April, 1962,

This information was made available to state or local health officials upon request. Repeated admonitions of toxicity have undoubtedly precluded any attempt to prescribe thalidomide to women in their childbearing years. Merrell has offered its scientific resources and cooperation to the FDA, the AMA and to other scientists working on this problem. A major portion of Merrell's research will be devoted to ascertaining the precise relationship between thalidomide and congenital malformations. Additional research is being conducted to determine the fundamental causes of phocomelia. Studies at the NINDB indicate that 1 in 16 newborn babies suffers a CNS defect. (No refs.)

11 North Lake Avenue
Sioux Falls, S.D.

1782 Bulletin on Narcotics. Ten years of the coca monopoly in Peru. Bulletin on Narcotics, 1962, 14, 9-17. [Editorial]

A comprehensive treatise focused on 10 years experience with various aspects of the Peruvian coca monopoly includes considerable statistical data with particular emphasis on the years 1958-1959 presented in tabular form. The Coca Monopoly acts to facilitate tax collection, and is largely responsible for production and sale of the coca leaf. Market stabilization has been achieved through the complex ramifications of the Monopoly. In 1948, the U.N. Commission of Enquiry on the Coca Leaf concluded that chewing of the coca leaf is harmful to health and to the economy, but that the habit cannot, like cocaine, be regarded as addiction in the medical sense. The committee further recommended limiting coca leaf production, controlling its distribution and eradicating the practice of coca leaf chewing. During the course of the working day, Indians are permitted to chew coca leaf at 2 specified 15-30 minute intervals. Coca leaf apparently provides abundant vitamins, relief from fatigue and diversion. The coca leaf mastication habit is not progressive, but is generally maintained for life at an average of 50 g of coca leaf per capita per day. (No refs.)

Department of Economic and Social Affairs
Division of Narcotic Drugs
United Nations
New York, N.Y.

1783 Shideman, Frederick E. The pharmacology of hypnotics and sedatives. I. South Dakota Journal of Medicine and Pharmacy, 1962, 15, 438-441, & 445.

In general, serious CNS depression results from administration of large doses of barbiturates, but depressant effects range from minimal sedation to anesthesia and coma, depending upon the dosage level. Sedative doses of these compounds are capable of impairing the functional capacity of the CNS. In hypnotic doses, barbiturates depress respiration only slightly, but more profound respiratory impairment occurs with increased dosages, due primarily to direct action on the medullary respiratory center. The barbiturates exert differential effects on various autonomic functions, including modification of the peripheral cardiac action of the vagus. Different barbiturates are bound in varying degrees to plasma albumin and other cellular proteins; pentobarbital and secobarbital are bound to the greatest extent, phenobarbital to a lesser degree and barbital the least. Acute and chronic intoxication with barbiturates has been widely recognized. Chronic intoxication mimics the signs and symptoms of chronic alcoholism, replete with grand mal seizures and psychotic behavior. (No refs.)

Department of Pharmacology and
Toxicology
University of Wisconsin
Madison, Wisc.

1784 Hoch, Erna M. Psychotropic drugs in the hands of the general practitioner. Antiseptic, 1962, 59, 113-119.

There are 3 major types of psychotropic drugs: tranquilizers (chlorpromazine), ataractics and thymoleptics, all of which are of value to general practitioners in India in treating patients with psychotic, neurotic or psychosomatic disorders.

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Indications and contraindications for various drugs are briefly explained. (No refs.)

Nur-Manzil Psychiatric Centre
Lucknow, India

1785 Pagani, F. Allucinogeni e tranquillizzanti. [Hallucinogens and tranquilizers.] *Gazzetta Medica Italiana*, 1962, 121, 121-124.

The chemical structures and pharmacological details were given for some tranquilizers and psychotomimetics: lysergide, mescaline, the chlorpromazine group, the reserpine group, amphetamines, benactyzine, etc. The role of various amines, particularly 5HT, in mental processes is also noted. (8 refs.)

Istituto di Chimica Farmaceutica e
Tossicologia
Università di Genova
Genoa, Italy

1786 Presse Médicale. Thalidomide et malformations congénitales. [Thalidomide and congenital malformations.] *Presse Médicale*, 1962, 70, 1241. [Editorial]

The worldwide spread of thalidomide syndrome is discussed with emphasis on the European situation. The laboratories which prepared thalidomide were among the 1st to suspect the possible role of thalidomide and they recalled it from the market in December, 1961. The necessity

for systematically investigating causes for all fetal malformation is underlined. (No refs.)

Presse Médicale
Masson & Cie.
Libraires de l'Académie de Médecine
120, Bd St.-Germain
Paris VI^e, France

1787 Lereboullet, Jean, Benoit, Philippe, & Ledoux, Michel. Médications nouvelles en psychiatrie. [New drugs in psychiatry.] *Revue du Praticien*, 1962, 12, 965-976.

Three drugs are detailed. Haloperidol, a nonphenothiazine, nonreserpine agent possessing the qualities of a major neuroleptic, its indications and uses (states of psychomotor excitation, delirious and confused states, particularly those related to hallucinations), tolerance and side effects and dosage schedules are discussed. The therapeutic indications (schizophrenia, chronic delirium, confusion states, thymic psychoses, melancholia and depression), dosage and techniques of administration, and side effects of thioridazine are reviewed. The pharmacology, therapeutic action, dosage schedules and side effects for chlordiazepoxide are outlined. Chlordiazepoxide apparently has superior tranquilizing properties to those of meprobamate and is devoid of properties particular to some neuroleptics, i.e., cataleptic properties and the inhibition of CR's. (No refs.)

[No address]

See also 1856, 1859

CLINICAL STUDIES

788 Boardman, R. H., Fullerton, A. G., Methell, M. S., & Conway, Stella. Intravenous procyclidine. *Lancet*, 1962, No. 239, 1131-1132.

Procyclidine (10 mg i. v.) was administered to 11 patients previously treated with chlorpromazine, trifluoperazine, reserpine and aloperidol who evinced 21 iatrogenic extrapyramidal disorders (dystonia 11, athetoid dyskinesia 4, parkinsonism 4, dyskinesia 1, oculogyric crisis 1). Procyclidine abolished the extrapyramidal disorders within 5 minutes in 12, in 20 minutes in 5, in 30 minutes in 1, and in 5 hours in 1. No extensive amelioration was observed in 3 instances, but some degree of improvement was observed within 5 minutes in all cases. No untoward effects were observed. Varying effects were observed in 4 patients with disorders of non-iatrogenic etiology.

Procyclidine (5 mg i. v.) reduced the frequency and amplitude of generalized violent involuntary movements in a patient with Huntington's chorea who was treated with perphenazine, 32 mg/day. Chorea-athetosis was ultimately controlled with 96 mg/day of perphenazine. Partial alleviation was obtained with procyclidine (10 mg i. v., 40 mg/day p. o.) in a patient with blepharospasm of unknown etiology. A woman with midbrain hemorrhage and decerebrate rigidity showed respiratory improvement 5 minutes after drug administration which persisted for 2 hours before death intervened. Dystonic tongue-protrusion secondary to arteriosclerotic parkinsonism was relieved within 5 minutes of procyclidine administration (10 mg i. v.). Intravenous procyclidine may be used to differentiate the dejected apathetic inertia of subclinical iatrogenic parkinsonism (due to phenothiazine accumulation) from a relapse of the illness. Mental confusion in 3 patients followed administration of procyclidine, 10 mg i. v., then 40-50 mg orally during the next 24 hours. A lower maintenance dose may obviate this effect.

Herrison Hospital
Dorchester, Dorset
Great Britain

89 Giddon, Donald B., & Lisanti, Vincent. Cholinesterase-like substance in the parotid saliva of normal and psychiatric patients.

Lancet, 1962, No. 7232, 725-726.

Parotid salivary cholinesterase was measured in 29 psychiatric patients (acute or affective schizophrenics) and 49 normal controls all with a median age of 24 years to detect diminutions in enzyme concentration in psychopathological states. In accordance with a modification of Ravin's method, 8-10 ml of parotid saliva was assayed in duplicate for titres of cholinesterase. Mean salivary cholinesterase in the patient group was 58% of that in the normal group, and salivary flow rate was lower and less variable. Patients exhibited either no measurable enzymic activity or values approximating those of controls. No enzyme was detectable in 7 patients. No correlations were found among the cholinesterase-like substance, flow-rate, Funkenstein test measures, physical characteristics, or diagnostic category for the entire group of patients. Enzyme concentration increased in 9 patients after i. m. injection of 10 mg methocholine. The relation of the parotid enzyme to stress was studied in a group of normal subjects twice weekly for 3 months who were then exposed to a variety of stressful experiences. No subject showed a correlation between enzyme concentration and parotid salivary flow rate. Apparently, both enzyme concentration and flow rate were controlled by the autonomic nervous system. Work by other investigators was also cited.

Harvard School of Dental Medicine
Boston, Mass.

1790 Schlosberg, Arié. Treatment of facial and head pain associated with depression. *Lancet*, No. 7237, 1962, 1027. [Letter]

A 50-year-old-woman presenting with depression and excruciating residual facial pain from trigeminal neuralgia unresponsive to retro-gasserian neurectomy received chlorpromazine (200 mg), methylphenidate (10 mg/day for 10 days) and imipramine (200 mg/day for 10 days). At discharge, her depression was alleviated, she was more active, her weakness disappeared and her facial pain was no longer intolerable. A maintenance dose of

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imipramine (75 mg) for 6 months has almost completely obliterated the pain.

Shalvata Psychiatric Hospital
Magdiel, Israel

1791 Gahagan, L.H., Intravenous atropine premedication before electroconvulsion therapy. *Lancet*, 1962, No. 7242, 1305.

A mixture of atropine (1.2 mg) and thiopental [dosage unspecified] is administered i.v. before ECT to prevent the undesirable cholinergic effects which are otherwise induced by ECT. Atropine premedication prevents cardiac arrhythmias of vagal origin and lessens internal secretion. Earlier experimental studies involved administration of double the above dosage, but the present amount suffices admirably. This premedication technique is a modification of the method of Hargreaves.

[No address]

1792 Beal, R.W., & Blackburn, C.R.B. The effect of nialamide on endogenously elevated blood ammonia levels in patients with liver disease. *Australasian Annals of Medicine*, 1962, 11, 19-23.

Twelve studies were carried out on 9 patients with elevated blood ammonia levels due to liver disease (8 cases) or uremia (1). As well a second group of 8 patients, all with chronic liver disease, was treated. In the 1st group, venous blood ammonia levels were determined before and 60-120 minutes after i.v. nialamide (100 mg) and in each study blood ammonia levels were significantly reduced, the reduction ranging from 18-75%. For the 2nd group, 1 to 1 1/2 hours after a standard meal containing about 30 g protein, an i.v. infusion of ammonium chloride was begun after the resting blood ammonia level was determined. When a significant elevation of arterial blood ammonia concentration was obtained, 100 mg nialamide was administered i.v. Arterial blood ammonia levels in this group were also significantly lowered. With the exception of 2 patients, the clinical effects of nialamide did not correlate with the great improvement in circulating ammonia levels.

Thus further study is in progress to determine the manner in which nialamide lowers both endogenously and exogenously elevated blood ammonia levels.

Clinical Research Unit
Royal Prince Alfred Hospital
Sydney, Australia

1793 Evans, Raymond D. The successful management of a case of neonatal tetanus using paraldehyde and promazine hydrochloride (Sparine) for sedation. *Archives of Pediatrics*, 1962, 79, 299-301.

Paraldehyde (1 ml i.m. every 4 hours) and promazine (5-12.5 mg i.m.) administered to a 2 or 3 week old female with neonatal tetanus produced complete relaxation and cessation of tonic spasms within 30 minutes. Maintenance therapy was continued for 14 days. Penicillin and tetanus antitoxin were also administered to preclude spastic activity and intercurrent infection. Mortality rates in neonatal tetanus are still universally alarmingly high. Other investigators have curtailed spasms with barbiturates, phenothiazine derivatives, chlorpromazine and thiopentone.

Fairbanks Medical & Surgical Clinic
Box 1330
Fairbanks, Alaska

1794 Alcock, N.S. Clinical evaluation of 1-methyl-5, 5-phenylethyl-hydantoin in the treatment of epilepsy. *Developmental Medicine & Child Neurology*, 1962, 4, 465-466.

1-Methyl-5, 5-phenyl-ethyl-hydantoin (100 mg/day increased weekly by 50 mg increments to obtain control) was administered to 89 epileptics aged 2 to greater than 14 years for 6 or more months in an effort to control seizure activity. Seizures were completely controlled in 43 of the patients, 75% reduction in seizures occurred in 16, 50% reduction in 15, and no response in 15. Improvement was shown by 51 out of 59 with grand-mal seizures and 5 out of 10 with petit-mal seizures. Skin rashes developed in 4 patients 10 to 14 days after

initiation of treatment. Excessive doses produced ataxia in 6 cases which disappeared upon decreased dosage. One patient evinced nystagmus which responded to drug discontinuation and steroid therapy. The best results were obtained with grand-mal epilepsy, and 6 of those with petit-mal seizures who improved were children approaching adolescence who may have improved spontaneously.

No address]

1795 Nilsson, E. Erfahrungen mit der Neuroleptanalgesie. [Experiences with neuroleptanalgesia.] Anaesthesist, 1962, 11, 17-20.

The author pretreated, 1 hour before the operation, 100, 50, and 100 patients, respectively, with the following combinations: 0.5 mg haloperidol plus 25 mg alimemazine plus 0.3 mg hydergin i.m.; 5 mg haloperidol plus 0.3 mg hydergin; and 10 mg haloperidol plus 0.3 mg hydergin. Only in the last group were there after-effects on the CNS, due probably to excessive haloperidol dosage. Anesthesia was begun with 2 mg phenoperidin i.v., followed by 20 mg phenoperidin, 2 mg haloperidol, and 0.3 mg hydergin in 500 cc of 5% glucose solution. Muscle relaxants were occasionally used. Patients could be brought to a suitable degree of analgesia without loss of consciousness. Recollections of the operative period were often exact. Patients reacted well to the trauma of surgery and their postoperative condition was very good, requiring only small amounts of analgesics.

Department of Anesthesia
University Hospital
Lund, Sweden

1796 Brown, Allan S. Die Neuroleptanalgesie mit Haloperidol und Phenoperidin als neues Narkoseverfahren für neurochirurgische Eingriffe, [Neuroleptanalgesia with haloperidol and phenoperidin as a new anesthetic technique in neurosurgery.] Anaesthesist, 1962, 11, 22-25.

A combination of haloperidol (up to 2.5 mg), phenoperidin (1-4 mg/hour), a muscle relaxant, nitrous oxide and oxygen (50:50)

was used in 82 neurosurgical operations (excluding intracranial operations with spontaneous respiration), and 33 angiograms and pneumoencephalograms. This combination proved highly successful, the patient being unconscious and areflexic during surgery, but returning to normal consciousness and reactivity levels within 2-5 minutes after discontinuation of nitrous oxide administration. As a result, the neurological course of the patient can be followed with the assurance that postoperative changes in responsiveness are due solely to changes in his neurological condition, and not to any depression caused by the anesthetic.

Department of Surgical Neurology
Western General Hospital
Edinburgh, Scotland
Great Britain

1797 De Castro, J., & Mundeleer, P. Die Neuroleptanalgesie. (Auswahl der Präparate, Bedeutung der Analgesie und der Neuroleptanalgesie). [Neuroleptanalgesia. (Drug selection, significance of analgesia and neurolepsy.)]. Anaesthesist, 1962, 11, 10-17.

The authors tested 12 different analgetic or neuroleptic drugs, employing 10 different treatment schemes, on about 8000 patients. The most effective combination was found to be a balanced method employing haloperidol and phenoperidin in dosage ranges of 2.2 - 5 mg and 2-15 mg, respectively, for adults. Succinylcholine (50 mg i.v.) may be added when required for muscle relaxation. Possible side effects include bronchial spasm, bradycardia, hypertension, tachycardia, etc. Reasons for these side effects and their prophylaxis and treatment are discussed. Nitrous oxide and oxygen can be used for maintaining anesthesia. Thiamine (0.5 - 1.0 g) has a favorable effect on respiration. Neuroleptanalgesia is less dangerous and less toxic than conventional general anesthesia.

Louis Caty Clinic
Baudour, Belgium

1798 Kapferer, J. M. Prinzipielle und praktische Überlegungen zur "Neurolept-analgesie". [Theoretical and practical considerations concerning neuroleptanalgesia.] *Anaesthesist*, 1962, 11, 25-28.

The theoretical principle underlying neuroleptanalgesia is separation of the different components, such as sleep, analgesia, muscle relaxation, and inhibition of reflexes. About 3100 patients were subjected to neuroleptanalgesia, using 50-300 mg thiopental for narcosis, which was maintained with N₂O (50-80%). Analgesia was provided by dextromoramide (2900 cases) or phenoperidine (200 cases), in doses of 1-1.5 mg/10 kg body weight. Muscle relaxation was obtained with small doses of succinylcholine or curare. An antiemetic effect was obtained with haloperidol (over 2900 cases) or methylperidol (over 200 cases) in doses of 0.5-5.0 mg i.v. at the start of narcosis. Side effects noted included dyspnea to apnea, which could be treated with N-allylnormorphine. Bronchial spasms can occur when phenoperidin is administered too rapidly, and can be counteracted by artificial respiration. Extrapyrimal disturbances can occur at too high (over 5 mg) doses of haloperidol or methylperidol, and can be controlled with barbiturates and promethazine. Dextromoramide can lead to addiction. The technique of neuroleptanalgesia is an improvement over older methods and not expensive.

No. 6 Sennstrasse
Innsbruck, Austria

1799 Junkenitz, Karl Walter. Insidon in der Allgemeinpraxis. [Insidon in general practice.] *Deutsches Medizinisches Journal*, 1962, 13, 358-359.

The piperazinoiminostilbene derivative iminostilbene (Insidon) was tested in 153 patients over a 6-month period at a usual dosage of 150-200 mg/day. Particularly good results were obtained in anxiety or insomnia due to emotional lability and lack of self confidence (67 cases), essential (not renal) hypertension (38 cases), climacteric and post-climacteric syndromes (26 cases), and migraine headache (22 cases). One example of each group is reported in detail.

The drug was well tolerated and side effects such as excitation and gastric distress did not appear below 300 mg/day.

Auweg 8
Baierdsorg/Mittelfranken
Germany

1800 Geller, Walter. Zur Entwicklung der Behandlung mit Monamino-Oxydase-Hemmer [History of the use of monoaminooxidase inhibitors.] *Nervenarzt*, 1962, 33, 124-129.

Following a chronological review of the development of the MAO inhibitors, comparative studies with iproniazid, phenelzine, nialamide (each approximately 25 cases), pheniprazine (50 cases) and isocarboxazid (over 80 cases) in the treatment of depression are reported briefly, indicating that isocarboxazid is the most effective and safest of these agents, no side effects having been observed in over 6 months' use at high dosages. This contrasts with the pronounced toxicity of iproniazid and the relative ineffectiveness of nialamide and phenelzine in severely depressed hospitalized patients; pheniprazine was effective for short periods of treatment but eventually produced side effects. Isocarboxazid was given in increasing doses from 20-40 to 60-100 mg/day, continued for at least 4-6 weeks (with a reduction in dosage at 2 weeks); maintenance treatment with 20 mg/day was effective. Many of the cases reported received concurrent imipramine, phenothiazines, thiaxanthenes and other preparations, but reserpine was excluded. Among 50 tabulated patients (30 depressives and 20 schizophrenics, including 3 hebephrenic and 2 catatonic), all 30 depressives responded satisfactorily, compared to only 9 schizophrenics; only 4 depressives and 14 schizophrenics required treatment for longer than 8 weeks. Side effects appeared in 7 cases (6 schizophrenics) and consisted mainly of circulatory disturbances such as tachycardia and hypotension. Isocarboxazid is thus indicated in all cases of lack of initiative, lethargy and catatonic depression; it is contraindicated in the presence of excitation, hallucinations or severe anxiety, whether of schizophrenic or manic-depressive origin.

Rheinisches Landeskrankenhaus
Bonn, Germany

1801 Lindner, Wilhelm, & Spiegelberg, Hedwig. Klinische Erfahrungen mit Triflupromazin. [Clinical experiences with triflupromazine.] *Medizinische Welt*, 1962, No. 10, 546-549.

Triflupromazine (initially 40 mg i.m. 3-5 times a day, then 200-400 mg/day p.o. and finally 75-200 mg/day p.o.) was tried in 49 female hospitalized patients, including 13 manic-depressives (11 manic), 7 schizophrenics, 2 with CBS, 2 with exogenous psychoses and 5 neurotics, over a period of 7 months. Most of the patients also received glutethimide, and treatment was continued for an average of 2-4 months. Good to excellent results were obtained within 5-10 days in 49 cases, and 21 more responded after more prolonged treatment; these were mostly severe involutional psychoses characterized by paranoia and hallucinations; 8 patients failed to respond at all. Side effects were fairly common, including infiltrations at the site of injection, extrapyramidal reactions and convulsive symptoms, but were readily controlled with glutethimide. The drug thus has a definite tranquilizing effect, producing normalization of mood and initiative at doses considerably lower than those of chlorpromazine. Its action resembles that of chlorpromazine without all of the side effects.

Psychiatrische Abteilung
Allgemeines Krankenhaus Ochsenzoll
Hamburg-Langenhorn, Germany

1802 Stelzer, H. Erfahrungen mit Sedapon in Geburtshilfe und Gynäkologie. [Experiences with Sedapon in obstetrics and gynecology.] *Medizinische Welt*, 1962, No. 6, 321-322.

Sedapon, a psychoautonomic regulator containing 150 mg meproamate, 2 mg yohimbine and 0.13 mg Belladonna alkaloids per tablet, was used in more than 400 obstetric and gynecologic patients over a period of 15 months. Among 54 patients suffering from nervous or autonomic complaints during pregnancy, 50 responded well to an initial dosage of 3-4 tablets/day, reduced 50% after 1-2 weeks and discontinued after 3-4 weeks. Hyperemesis gravidarum was controlled successfully in 24 of 32 patients

by 2-4 tablets/day and 6 more responded after addition of vitamins. Sedapon was also used before and during labor in 355 cases, with good effects on anxiety and agitation. The drug also shortened the first stage of dilatation, and had no effect on the fetus. Sedapon is also indicated in spastic or inflammatory pelvic disease, chronic constipation, menopausal syndromes (when hormones are contraindicated) and the premenstrual syndrome (good response in 24 of 29 patients at 3-4 tablets/day).

Frauenklinik Düsseldorf
Düsseldorf, Germany

1803 Roth, G. Elektrencephalographische Beobachtungen bei Anwendung von Thalidomid. [Electroencephalographic observations using thalidomide.] *Nervenarzt*, 1962, 33, 130-133.

Thalidomide (200 mg p.o. or rectally in adults, half that in children) was used for diagnostic purposes to provoke disturbances in the EEG in 60 patients with epilepsy (13 cases), cerebrovascular disease (14 cases), postencephalitic syndromes (4 cases), posttraumatic syndromes (6 cases), autonomic disturbances (9 cases), psychoses and neuroses (11 cases), Little's disease, multiple sclerosis and drug intoxication (1 case each). The 24 patients showing convulsive symptoms are tabulated in detail. Thalidomide had a marked activating effect in 6 of these 24, a moderate effect in 5, little or no effect in 12, and a normalizing effect on 1 case of paroxysmal dysrhythmia; the greatest effect was obtained on essentially normal EEG's. Several examples are given. The use of thalidomide is superior to other methods in that there is no β -activation and no clinical excitation.

II. Neurologische Abteilung
Nervenheilanstalt Wien-Rosenhügel
Vienna, Austria

1804 Anton, Alfred. Ergebnisse einer klinischen Prüfung des Neuroleptikums Ciatyl. [Results of a clinical trial of the neuroleptic drug Ciatyl.] *Medizinische Welt*, 1962, No. 12, 665-669.

Ciatyl, a chlorperphenthixene closely related to perphenazine, was tested in 115 hospitalized psychiatric patients suffering from a variety of acute and chronic psychoses. Initial dosage was usually 150 mg/day i.m. (occasionally first 25 mg i.v.), gradually reduced to 50 mg/day p.o. Four illustrative cases are reported in detail. The results indicate that Ciatyl is a highly effective neuroleptic with a true antipsychotic action which far exceeds the sedative effect of bromine and barbiturates. It is particularly indicated in acute psychotic agitation, anxiety and psychomotor excitation. The drug is less effective in defective psychoses with loss of contact and initiative, but even here it facilitates hospital care, and can advantageously be combined with thymoleptics in cases of severe endogenous depression. Ciatyl is well tolerated, and the occasional extrapyramidal reactions, muscular dystonia and hypotension can readily be controlled. Marked drowsiness is common at the beginning of treatment.

Westfälisches Landeskrankenhaus
Münster, Germany

1805 Gómez-Reino y Filgueira, J., & Fernández Vicente, L. Nuestras experiencias con el "Meleril" en la mania endógena y en las esquizofrenias paranoideas crónicas. [Our experience with Melleril in endogenous mania and in chronic schizophrenic paranoia.] *Actas Luso-Españolas de Neurología y Psiquiatría*, 1962, 21, 159-164.

Thioridazine (Melleril), 200-400 mg/day, was used in the treatment of 7 cases of endogenous mania. Excellent results were obtained in 5 cases and good results in 2. Twenty-one schizophrenics were treated for 2-6 months with 400-600 mg thioridazine daily. Excellent improvement (remissions) occurred in 15.7% of 19 paranoid schizophrenics, good results were obtained in 21% and mediocre results in 5.2%; 1 case of hebephrenic schizophrenia and another of simple schizophrenia showed only mediocre improvement. Target symptoms particularly susceptible to chemotherapy were hyperexcitability, hallucinations, ideas of reference (prejudicial, autoaccusatory, etc.), anxiety and depression. Improvement for

all cases reported was 36.7%. No side effects except slight drowsiness were observed in any patients.

Sanatorio Psiquiátrico de Toen (P.A.N.A.)
Orense, Spain

1806 Vintimilla Alborno, Jaime. La amitriptilina en el tratamiento de las depresiones endógenas. [Amitriptyline in the treatment of endogenous depressions.] *Antioquia Medica*, 1962, 12, 494-501.

Fifty cases of endogenous depression, 30 hospitalized and 20 ambulatory, were given amitriptyline, either 25 mg tablets orally or 10 mg parenteral injections. Usual dosage was 25 mg t.i.d., raised to as much as 150 mg per day when necessary. The treatment period ran from 1-5 months. Thirteen cases had concomitant ECT, 8 cases chlorpromazine and 4 patients required psychotherapy. The only side effect was 1 case of nausea. In 14% the results were excellent, in 30% good, in 30% fair, in 12% poor and in 14% uncertain.

Hospital Mental de la Beneficencia de
Antioquia
Medellín, Colombia

1807 Merlis, Sidney, Turner, William J., & Halpern, Seymour. Chlordiazepoxide as adjunctive therapy in convulsive disorders. *American Journal of Psychiatry*, 1962, 119, 575-576.

Chlordiazepoxide (10-60 mg/day p.o.) was administered to 86 epileptics aged 5-66 years alone or in combination with standard anticonvulsants for periods of up to 16 months. Evaluation included serial EEG's (in 30 patients) and clinical observation. Side-effects ensued in 43 cases: 17 evinced somnolence, 7 ataxia, 5 vertigo, 5 irritability, 2 restlessness, 2 fatigue and 1 each headache, leucopenia, insomnia, facial flushing and jaundice. Before treatment, 89% had fair or poor control of seizures, whereas only 66% had fair or poor seizure control after the introduction of chlordiazepoxide. Chlordiazepoxide is apparently efficacious as an adjunctive

treatment in the control of epileptiform seizures.

Research Division
Central Islip State Hospital
Central Islip, N. Y.

1808 Haydu, George G., Dhrymiotis, Andreas, & Quinn, Gertrude P. Plasma imipramine level in syndromes of depression. *American Journal of Psychiatry*, 1962, 119, 574-575.

Plasma imipramine levels were determined 2, 4 and 7 hours after 100 mg of imipramine was administered p.o. to 8 patients with psychotic depressive syndromes. Subsequently, imipramine (50 mg t.i.d.) was administered for 4 weeks, after which plasma imipramine levels were again determined in 4 patients who responded to drug therapy and 4 who proved refractory. Plasma determinations 7 hours after the single oral dose differed significantly in the 2 groups at the 5% level, and this difference was maintained during therapy. A similar distribution was obtained after 50 mg dose was administered i.m. Those who responded to therapy consistently manifested lower plasma imipramine levels than did the refractory group. Measurement of 24 hour urine and feces imipramine excretion exhibited a similar trend. By way of explanation, the organ affinity of imipramine may vary according to the functional state of the CNS as modified by a particular psychopathology. The refractory patients showed schizoid pathology while those responding to treatment were of a melancholic type. Differential drug distribution and binding rather than insufficient absorption may have precipitated the discrepancy observed in plasma levels.

Creedmoor State Hospital
Queens Village, N. Y.

1809 Masera, Alvaro. Contribuição ao emprego da flufenazina em geriatria. [Contribution to the use of fluphenazine in geriatrics.] *Revista Brasileira de Medicina*, 1962, 19, 348-352.

Twenty patients, aged 50-85 years, with various problems of social adjustment (anxiety and tension) were treated with

fluphenazine for 2 months. Most manifested psychosomatically influenced digestive or cardiocirculatory disorders. Five patients received 2 mg/day p.o. for the 1st month and 1 mg/day for the following month. All the rest received 1 mg/day, and 2 patients received medication for 45 days. Improvement in 80% of the cases was considered excellent. No toxicity was evidenced; this was true even in a patient with auricular fibrillation who was 84 years of age. However, 1 patient showed drowsiness with nausea and another drowsiness with depression during treatment for 45 days.

IPASE
Pôrto Alegre, Rio Grande do Sul
Brazil

1810 Mans, J.-P., & Cornil, J. Résultats d'une année d'expérimentation d'un nouveau neuroleptique, le chlorhydrate de prothipendyl, en psychiatrie. [The results of a year's psychiatric experimentation with a new neuroleptic: prothipendyl chlorhydrate.] *Annales Médico-Psychologiques*, 1962, 1, 120, 637-638. [Abstract]

In the treatment of 39 cases, prothipendyl [dosage unspecified] appeared to have good sedative and neuroleptic action without the production of side effects. Used initially in agitated states the drug is not as potent as chlorpromazine, but still useful. (No refs.)

[No address]

1811 Misrahi, R., Joubert, P., & Bernard-Bouissières. Utilisation du niamide dans le traitement des troubles digestifs psychosomatiques et plus particulièrement: la rectocolite hémorragique. [The use of Niamide in the treatment of psychosomatic digestive disturbance, particularly, hemorrhagic rectocolitis.] *Annales Médico-Psychologiques*, 1962, 1, 120, 630. [Abstract]

Three cases of hemorrhagic rectocolitis improved in 3 months of treatment with nialamide (Niamide) [dosage unspecified].

[No address]

1812 Fouks, L., Laine, P rivier, Boucher, Mathis, Ferrant, & Riou. Rapport sur l'essai clinique du S. 186 (Hexa-cyclonate de sodium). [Report on a clinical trial of S. 186 (sodium hexa-cyclonate).] Annales M dico-Psychologiques, 1962, 1, 120, 636. [Abstract]

Hexacyclonate, 25-150 mg/day, improved the general and cardiovascular tone, as well as alertness and mental efficiency of patients. The drug is recommended for use in arteriopathic senile states and also in childhood oligophrenia, particularly in cases of apathy. It is contraindicated in the presence of convulsive tendencies.

[No address]

1813 Reichle, Claus W., Smith, Gene M., Gravenstein, Joachim S., Macris, Spyros G., & Beecher, Henry K. Comparative analgesic potency of heroin and morphine in postoperative patients. Journal of Pharmacology and Experimental Therapeutics, 1962, 136, 43-46.

The subjective reports of 522 patients with steady incisional pain due to surgery were used to compare the analgesic power of heroin and morphine (double-blind basis). Morphine, 10 mg/70 kg, was used as a standard in an evaluation of pain relief produced by 4 different dosages of heroin: 6, 4, 2, and 1 mg/70 kg. Heroin was approximately 2-4 times as potent as morphine in pain relief during the 1st 150 minutes after injection. At 45 minutes equianalgesic doses of heroin, compared to morphine, for moderate, severe and very severe pain, were 3.2, 2.3 and 3.9 mg, respectively. The corresponding values 90 minutes after medication were 4.0, 4.3 and 4.4 mg and those at 150 minutes 3.7, 5.2 and 4.8 mg.

Anesthesia Laboratory
Harvard Medical School
Massachusetts General Hospital
Boston, Mass.

1814 Walsh, P.J.F. Compulsive shouting and Gilles de la Tourette's disease. British Journal of Clinical Practice, 1962,

16, 651-655.

A 29-year-old man with Gilles de la Tourette's disease (compulsive shouting with motor tics and compulsive utterances) coupled with mental coprolalia received chlorpromazine (50-200 mg t.i.d. for 6 weeks, then 25 mg t.i.d. for maintenance) and evidenced a remarkable degree of improvement. He had previously received trifluoperazine, imipramine [dosage unspecified for both drugs], chlorpromazine (50-200 mg t.i.d. for 2 weeks) and ECT, all to no avail. The 2nd trial of chlorpromazine resulted in resocialization, cessation of shouting and disappearance of tics. A diagnosis of schizophrenia was suspected but never corroborated. Several cases culled from the literature are cited, with the suggestion that some underlying organic defect may predispose toward development of Gilles de la Tourette's disease.

[No address]

1815 Hofmann, Volker. Behandlung der spastisch-hypertrophischen Pylorusstenose mit Promazin und Eumydrin. [Treatment of spastic-hypertrophic pyloric stenosis with promazine and atropine methyl nitrate.] M nchener Medizinische Wochenschrift, 1962, 104, 463-465.

A combination of promazine (2-4 mg q.i.d., p.o. or 3-5 mg t.i.d. or q.i.d., i.m.) and atropine methyl nitrate (Eumydrin; 1-3 drops of 1% alcoholic solution, p.o., 4-6 times a day) was used in the treatment of 57 infants (average age 32.3 days) with spastic-hypertrophic pyloric stenosis over a 2 1/2-year period. Along with proper diet and supportive measures, this treatment was very effective and none of the infants died. Vomiting stopped, body weight began to increase, and treatment could be interrupted after 5-9 weeks. Although there were 2 cases of pneumonia and 5 of pyuria, as well as other complications, there were no side effects attributable to the drugs and the dosage of atropine could be kept at low levels due to the potentiating effect of promazine.

St dtische Kinderklinik
Augsburg, Germany

1816 Gürtler, J. Zum Problem der Schlaflosigkeit im Sanatoriumsbetrieb. The problem of insomnia in patients with tuberculosis.] Praxis, 1962, 51, 136-138.

Vesparax, a new combined preparation containing 150 mg secobarbital, 50 mg bromlobarbitol and 50 mg hydroxyzine per tablet, was tried as a hypnotic in 100 sanatorium patients at a dosage of 1/4 tablet per day. Questionnaires showed that 78-98% of the patients experienced deep, essentially dreamless sleep beginning within 30 minutes of retiring and lasting over 7 hours, but from which they could readily be awakened. The only side effects were slight drowsiness and dry mouth in 4-6%. The dosage was established on the basis of the author's personal experience with Vesparax (up to 1 tablet) and control studies with hydroxyzine (25-50 mg) and chlordiazepoxide (20 mg) in 10 patients each. These showed that hydroxyzine alone is an excellent tranquilizer but is insufficient to control insomnia, and that more dreams are produced by chlordiazepoxide.

St. Gallisches Sanatorium
Knoblisbühl-Walenstadtberg, Switzerland

1817 Gripwall, Erik. Ett nytt fentiazin-derivat—thioridazin. [A new phenothiazine derivative—thioridazine.] Nordisk Medicin, 1962, 68, 1167-1168.

Eighty-two patients were given 30-400 mg, most often 35-100 mg, of thioridazine. Treatment lasted from 5 to 70 days. The main symptoms were agitation, anxiety, tension and insomnia. Positive results were obtained in more than 65% of the cases. The drug had a tranquilizing effect on increased psychosomatic activity and tension. Side effects were negligible. Thioridazine appears to be a superior drug in ambulatory practice.

Centrallasarettet
Medicinska avdelningen
Södertälje, Sweden

1818 Wickström, Lennart, & Hahn, Nils. β -Fenylisopropylhydrazin (Catran) vid schizofreni. [β -Phenylisopropylhydrazine

(Catran) in schizophrenia.] Nordisk Medicin, 1962, 68, 1165-1167.

One-hundred-and-ninety-five patients, diagnosed as schizophrenic, were treated with pheniprazine (β -phenylisopropylhydrazine; 6-15 mg/day for 7 months). After 2 weeks dosages were reduced to a daily maximum of 12 mg. Phenothiazine derivatives were administered concomitantly. Fifty-eight percent of the cases improved. The drug was especially effective against depressive characteristics and secondary hallucinations. In 6 cases treatment was interrupted because of side effects: jaundice in 1 and considerably increased transaminase values in 5 cases.

Birgittas sjukhus
Vadstena, Sweden

1819 Kaartinen, Matti. Kliniska erfarenheter av klorprothixen. [Clinical experiences with chlorprothixene.] Nordisk Medicin, 1962, 68, 1161-1164.

Two-hundred-and-eighty-two patients (schizophrenia, mania, depression, involutional psychosis, senile psychosis, neurotic reactions, alcoholism, aggressive oligophrenia and epilepsy) were treated; 172 with chlorprothixene only (15-600 mg p.o. usually t.i.d.). The 110 other patients received chlorprothixene and insulin coma, ECT, reserpine and/or imipramine. Overall results were satisfactory; about 85% could be sent home or were obviously improved. Psychomotor agitation, restlessness, insomnia, anxiety, apathy, withdrawal and hallucinations showed the best improvement. The effect on delusions, neurotic depressions and cases of senile confusion was not as good. No effect was observed in endogenous depression. Side effects were: orthostatic vertigo and collapse, tachycardia and allergic dermatosis. Treatment had to be interrupted in 10 cases. Also, an unsuccessful suicide attempt is described where 2000 mg of chlorprothixene was ingested.

Distriktssjukhuset
Halikko, Finland

Clinical Studies
Abstracts 1820-1823

1820 Lapinsohn, L.I. Anabolic steroids in the treatment of psychiatric states. (Effect of oxymetholone). Diseases of the Nervous System, 1962, 23, 226-230.

Following a detailed presentation of the underlying concepts in the design of the study and a review of the general indications and contraindications for oxymetholone, the results of a study of the adjuvant use of this compound in 3 groups of psychiatric patients are briefly reported. The drug was administered at a dosage of 2.5 mg t.i.d., p.o. in 3 courses of 3 weeks each, with 1-week intervals, in combination with other types of treatment, to a total of 52 patients evaluated by 3 different investigators. Excellent results were obtained in 10 of the 43 schizophrenics and 1 case of posttraumatic encephalopathy. Good results were obtained in 21 schizophrenics, 2 involutional psychoses, 1 phobic reaction and 1 postpartum psychosis. Fair results were obtained in 11 other schizophrenics, while 4 anxiety states and 1 schizophrenic showed no change. Oxymetholone thus has considerable value as an adjuvant in the treatment of certain psychiatric conditions.

Psychiatry and Neurology Service
VA Hospital
Coral Gables, Fla.

1821 Müllender, H. Atarax in der Geburtshilfe. [Atarax in obstetrics.] Praxis, 1962, 51, 475-476.

Hydroxyzine (Atarax; 100 mg i.m. at the beginning of dilatation, repeated in 30 minutes) was tested in a double-blind study on 90 parturient women, including 43 primiparas and 47 multiparas. Hydroxyzine produced good effects in 21 and moderate effects in 19 out of 46 patients, and reduced the consumption of pethidine 30%, while the placebo produced good effects in 12 and moderate effects in 7 out of 44 patients. There were 4 surgical deliveries in each group and no apparent effects on the fetus.

Frauenklinik des Kantonsspitals
St. Gallen, Switzerland

1822 Gershon, Samuel, Holmberg, Gunnar, Mattsson, Eira, Mattsson, Nils, & Marshall, Arthur. Imipramine hydrochloride. Its effects on clinical, autonomic and psychological functions. Archives of General Psychiatry, 1962, 6, 96-101.

Psychiatric and clinical observations (Gorsham Ward Behavior Scale and MSRPP), psychological studies (Identical Forms, Bourdon Dot Cancellation, Stroop Color Naming, Interpretation of Facial Expressions, Rod and Frame, Reaction Time to Visual Stimulus, Mirror Drawing, Digit Span and Color-Form Movie) and studies on the autonomic nervous system (ECG and blood pressure response to levarterenol, epinephrine, methacholine or yohimbine) were carried out before and after treatment with imipramine (3 mg/kg/day p.o. for 3 weeks) in 30 patients, including 15 chronic schizophrenics, 7 with non-schizophrenic psychoses (mostly CBS), and 8 neurotics (5 sociopaths and 3 alcoholics). Imipramine was found to produce activation of the psychotic process, with increased aggressiveness, hostility and hallucinatory phenomena, in nonschizophrenic and mildly schizophrenic psychotics, while having little effect in very deteriorated schizophrenic or nonpsychotic patients. It potentiated the pressor and hypotensive effects of levarterenol and methacholine, respectively, and both the psychic and autonomic effects of yohimbine, but had little effect on response to epinephrine. Performance on psychological tests was somewhat, but not markedly, improved.

Schizophrenia and Psychopharmacology
Research Project
Ypsilanti State Hospital
Ypsilanti, Mich.

1823 Bürger, H.H. Die Re-Aktivierung der Psyche als medikamentöses Problem unter Berücksichtigung von Erfahrungen mit dem Psychotonikum Captagon. [Psychic reactivation as a pharmacological problem with reference to experiences with the psychotonic drug Captagon.] Medizinische Welt, 1962, No. 9, 493-496.

A group of 137 hypoactive, anergic and

Depressive patients received Captagon, 10-100 mg in the morning, followed by 10 mg in the afternoon. Side effects were generally harmless and transitory, consisting, in order of frequency, of palpitation and a feeling of pressure surrounding the heart, sensations of pressure, pulsation, and warm flushes in the region of the head, dizziness, and mild nausea, all probably due to the slight hypotensive effect of the drug. Occasional hand tremors, and a strong need to urinate were also experienced. The drug is indicated as a substitute for amphetamine in symptomatic treatment of drive diminution, when the latter is contraindicated. It has been found especially useful in the treatment of older patients.

Medizinische Abteilung
Krankenhaus Mariahilf
Hamburg-Harburg, Germany

1824 Gross, Heinrich. Der Anwendungsbereich von Nialamid (Niamid) in der klinischen Psychiatrie. [The range of application of nialamide (Niamid) in clinical psychiatry.] *Medizinische Welt*, 1962, No. 11, 613-617.

Nialamide was administered p.o. in doses of 75 mg/day to 141 depressed male patients. No side effects were noted at this dosage, but dizziness, headache, nausea, insomnia, and tremor were experienced with higher doses. Blood pressure declined by 10-20 mg Hg, but no cases of orthostatic collapse were recorded. About 1/3 of the cases were treated for approximately 3 weeks, and the remainder were treated for periods up to 8 months. Nialamide had a clear stimulatory effect in exogenous depressive conditions, and some patients were able to be discharged. Only milder cases of endogenous depression can be treated effectively. Generally speaking, the drug is effective in reactive depression, and neurotic and senile depression, however, approximately 1 week must elapse before beneficial effects are manifested. Nialamide is not sufficiently effective in severe depressions with vital inhibition, suicidal tendencies, hypochondria and agitation to replace ECT or isocarboxazid treatment.

Schizophrenia is only slightly improved.

Heil- und Pflegeanstalt "Am Steinhof"
Vienna, Austria

1825 Flegel, Horst. Psyquil im Psychiatrischen Krankenhaus. [Psyquil in the psychiatric hospital.] *Medizinische Welt*, 1962, No. 2, 99-102.

A total of 70 female patients was treated with triflupromazine (Psyquil) over a 1-year period at an oral dosage of 30-75 mg per day initially, increasing to 150 mg/day, if no improvement was evinced at the lower doses. Of the 60 schiziform patients, 24 were discharged, but 6 of these relapsed after 1-5 months. In addition, 7 others improved sufficiently to be kept in open wards, while 19 more, although restricted to locked wards, could be assigned to work therapy. Side effects, noted in 14 patients, consisted of stupor, pallor, weakness, excessive perspiration, tachycardia, and a tendency to collapse. Parkinsonian symptoms were displayed by 29 patients. Triflupromazine is effective in the treatment of schizophrenia of long duration, and the side effects can be readily controlled.

Rheinisches Landeskrankenhaus
Düsseldorf, Germany

1826 Flegel, Horst. Zur Dokumentation und Auswertung psychiatrisch-klinischer Verlaufsgegebenheiten für die Erprobung von Psychopharmaka anlässlich Thioridazin-medikation. [Documentation and evaluation of data from the psychiatric clinic in the testing of psychotropic drugs, with particular reference to thioridazine.] *Nervenarzt*, 1962, 33, 112-116.

A group of 80 women, including 55 schizophrenics and 12 depressives, was treated with thioridazine over a 2-year period with dosages of 75 mg and more per day. There was no clear relationship between dosage and percent discharged. Chronic schizophrenic patients could not be discharged after treatment with the drug, but the treatment proved effective in 10 out of 20 cyclic schizophrenics with a history of

previous acute attacks. Also, 4 depressives could be discharged. Relapses occurred in 2 cases. Of the remaining cases, 19 improved to the point where they could be assigned to work therapy. Side effects included lassitude, dizziness, tachycardia, gastric discomfort. One case of jaundice, in a patient previously treated with another phenothiazine derivative, was cured after withdrawal of the drug. Other symptoms were edema (in an edema-prone patient) and acne. Most symptoms disappeared after a 2-month period. Thioridazine is indicated for the treatment of more or less chronic psychoses. Severe agitation and acute psychotic syndromes require more powerful drugs. Psychopathic excitability is also controllable with thioridazine.

Rheinisches Landeskrankenhaus
Düsseldorf, Germany

1827 Barron, David W., & Dundee, John W. Clinical studies of induction agents. I: A comparison of the incidence of induction complications with nine barbiturates in electroconvulsive therapy. *British Journal of Anaesthesiology*, 1962, 34, 90-94.

Nine barbiturates: thialbarbital, thiamylal, Inactin, buthalital, methitural, hexobarbital, methohexital and B. 137 were administered to 1010 patients (average age 39-45 years) as anesthesia for ECT 1 hour after atropine (0.65-1.3 mg) premedication and 1 minute before administration of suxamethonium. Resultant complications included excitatory phenomena (muscle tremor, twitchings and other involuntary muscle movement) and respiratory upset (coughing, hiccoughing and laryngospasm). Administration of anesthesia was assessed and graded according to the scheme designed by Dundee (1961). Hexobarbital, methohexital and B. 137 caused a significantly higher incidence of excitatory phenomena than thiopental. Although the incidence with Inactin was greater than that for thiopental at a 2% significance level, it was not different from that associated with thialbarbital, thiamylal, buthalital or methitural ($p > 0.05$). Administration of buthalital and methitural was associated with a much higher incidence of respiratory upset than that which appeared

with any of the other drugs. Seven of the above drugs were administered to 22 patients, and no respiratory aberrations were manifested, although hexobarbital and methohexital once again evinced excessive excitatory phenomena. An identical dose of thiopental and thiamylal was administered to 26 patients, and no complications ensued from either drug. Inactin (average dose 4.07 mg/kg) and B. 137 (average dose 3.71 mg/kg) were administered to 44 patients. Excitatory phenomena occurred in 6 patients with Inactin and in 13 with B. 137, but the difference between dosages failed to reach accepted levels of significance. Hexobarbital (average dose 4.93 mg/kg) and thialbarbital (5.79 mg/kg) were given to 32 patients. Excitatory symptoms occurred in 14 receiving hexobarbital and 1 given thialbarbital, with a highly significant difference ($p < 0.01$). The thiobarbiturates produced a low incidence of side effects and a high incidence of respiratory upset, while the methylated barbiturates produced a high incidence of excitatory phenomena.

Department of Anaesthetics
The Queen's University of Belfast
Great Britain

1828 Svendsen, B. Borup, Faurvy, A., & Kristjansen, P. Sammenligning af thioridazin og klorpromazin over for kroniske skizofrene psykoser under anvendelse af placeboteknik. [Comparison of thioridazine and chlorpromazine in chronic schizophrenia using a placebo technique.] *Nordisk Medicin*, 1962, 67, 390.

In a double-blind crossover study 61 chronic schizophrenics received thioridazine or chlorpromazine for 12 weeks followed by 16 weeks of therapy with the alternate preparation. There were 9 dropouts. Thioridazine was similar in effectiveness to chlorpromazine. In cases where chlorpromazine produces extrapyramidal symptoms and/or a rash, then thioridazine is indicated. Some patients improved optimally on one drug, some on the other.

[No address]

1829 Belling, G., & Kronholm, V.
Isocarboxazid-behandling af depressioner.
[Isocarboxazid therapy in depression.]
Nordisk Medicin, 1962, 67, 392.

Twenty-five cases of endogenous depression were treated with 10 mg isocarboxazid t.i.d. which was increased after 3 days to 20 mg t.i.d. After a change in symptomatology had appeared dosage was gradually reduced to 10-20 mg/day. If no remission was observed after 3 weeks, then ECT was employed. Eight out of 25 patients were cured in 10-20 days. After 3 weeks 8 patients had improved, but insufficiently, and 9 remained unchanged. After 10 days 14 out of 25 patients showed dizziness due to orthostatic hypertension. Insomnia, headache and enuresis were also noted as side effects. Treatment was considered satisfactory in about 25%.

[No address]

1830 Iisalo, Esko. Monoaminooxidas-hämmare vid ulcerös colit. [Monoamine oxidase inhibitors in ulcerative colitis.]
Nordisk Medicin, 1962, 67, 219-221.

Six out of 9 ulcerative colitis patients improved on 30 mg/day isocarboxazid with 37.5-100 mg/day nialamide or nialamide treatment combined with salazosulfapyridine cortisone therapy.

Turun Yliopisto
Medicinska Kliniken
Abo, Finland

1831 Riddoch, Margaret E. Evaluation of phencyclidine (CI-395) for premedication of children. Anaesthesia, 1962, 17, 419-421.

Phencyclidine (1.5 mg/14 pounds i.m.) and atropine (0.4-0.6 mg) were administered to 38 children aged 2-11 years 1 hour before minor surgery. Each child's state was then assessed and classified as calm, disturbed or turbulent. A previous study comparing phencyclidine with atropine, nembutal, pethidine, trimeprazine, etc. as a preoperative sedative revealed that although phencyclidine was a more effective premedication than all other widely used

agents, it produced a higher proportion of disturbed and turbulent children post-operatively than all other drug combinations except pentobarbital and atropine. Approximately 25% of the phencyclidine-treated patients observed preoperatively exhibited signs of emotional upset ranging from nausea and dizziness to agitation, extreme restlessness and delirium. About 50% of the children who appeared calm seemed completely detached and were quite phlegmatic about accepting an inhalational induction. Such serious side effects necessitated abandonment of phencyclidine as a premedicant.

The Royal Infirmary
Aberdeen
Great Britain

1832 Camilleri, Joe G. The use of phencyclidine (LI-395) in obstetric procedures. Anaesthesia, 1962, 17, 422-426.

Pethilorfan or pethilorfan combined with promethazine [dosage unspecified] was administered to 15 pregnant women within 4 hours before delivery, after which atropine (0.6 mg) and phencyclidine (10-15 mg) were given i.v. as premedication. Complete analgesia supervened within 3-6 minutes of injection, and lasted 30-45 minutes during which various obstetric procedures were performed without any discomfort to the patient. During the period of analgesia, the patient remained in a catatonic trance, staring fixedly into space. During obstetric procedures, the respiratory rate, pulse and blood pressure all rose slightly. No vomiting occurred before or after the procedure, and uterine contractions proceeded normally. Cyclopropane was used supplementally in 2 cases which required more extensive surgical procedures. No deleterious effects were observed in the babies thus delivered. Phencyclidine is highly recommended for use in obstetrics.

The Central Middlesex and Willesden
General Hospitals
Middlesex
Great Britain

1833 Joseph, Samuel R. Combined anti-depressant tranquilizer therapy in somatic and psychosomatic illnesses. *Arizona Medicine*, 1962, 19, 239-241.

Sixty-two ambulatory patients, aged 22-81 years, suffering from both anxiety and depressive symptoms were treated with a combination of trifluoperazine and tranlycypromine for 3 months to 1 year. The usual dosage was 1-2 mg trifluoperazine b.i.d. and 10 mg tranlycypromine b.i.d. In 15 patients, the symptoms were associated with organic disease including arthritis, asthma, etc. Response was rated as excellent in 27%, good in 39%, fair in 13% and poor in 21%. No serious toxicity was encountered. Side effects in 19 included insomnia, dry mouth and drowsiness, which disappeared upon dosage reduction or cessation of the combination therapy. Distress was relieved in patients suffering from organic disease; all were better able to relate and gain insight.

2021 North Central Avenue
Phoenix, Ariz.

1834 Kristensen, Keety Kjaerbye. Libriumbehandling af angstneuroser. [Librium therapy in neurotic anxiety reactions.] *Nordisk Medicin*, 1962, 67, 392-393.

Twenty-five patients, average age 37 years, were given 30-80 mg chlórdiazepoxide daily (occasionally up to 150 mg/day), dosage was progressively increased to about 200 mg/day. One patient was cured spontaneously, 3 showed decided improvement, 12 some improvement, 7 remained unchanged, 1 worsened and 1 committed suicide. No toxicity was observed. Drowsiness was seen in about half the case load, disappearing on reduced dosage. One patient had fainting spells, 1 erythema and 3 euphoria. Chlórdiazepoxide may be expected to compete with meprobamate in ameliorating mild neuroses.

[No address]

1835 Kammerer, Th., Singer, L., Geissmann, P., & Wetta, J.-M. Utilisation

d'un nouveau neuroleptique: la tétrabénazine. Résultats cliniques, biologiques et électro-encéphalographiques. [The use of a new neuroleptic: tetrabenazine. Clinical, biological and electroencephalographic results.] *Annales Médico-Psychologiques*, 1962, 1, 120, 106-115

Seventeen paranoid schizophrenics, (8 suffering delirium and 4 with chronic hallucinatory psychosis), aged 20-60 years, were treated for 3-7 weeks with tetrabenazine (average daily oral dose 90-135 mg). The doses were progressively augmented and usually given t.i.d. Tetrabenazine had a marked clinical action against hallucinations; in acute psychoses it had an immediate activity against anxiety, confusion and panic states in patients; in chronic psychoses delirium was diminished and patients adjusted better to reality. Encephalographically, disturbances were noted which contraindicated the drug in cases of epilepsy or in subjects with a tendency towards epilepsy. Tolerance to tetrabenazine was highly variable and side effects notable, i.e., typical extrapyramidal syndrome. Untoward effects included moderate hypotension, dry mouth (in almost all patients), drooling, anorexia, constipation, daytime somnolence (especially in the 1st week of treatment), fine tremor and agitation. Some of these effects were partially controlled by barbiturate administration.

[No address]

1836 Mathisen, H. Storm. Hypertensjonsbehandling med monoaminooxydase-hemmer og decarboxylasehemmer. [The treatment of hypertension with MAO and decarboxylase inhibitors.] *Nordisk Medicin*, 1962, 67, 459.

Thirty-seven hypertensive patients were treated with serine-N²-isopropylhydrazine (RO4 1038) and 10 with the decarboxylase inhibitor α -methyl-dopa. Also placebo effect was assayed as a control for the latter drug. α -Methyl-dopa was used for some days (0.5-2 g/day) without effect followed by RO4 1038 (usual dosage 15-20 mg/day). Both preparations lowered blood pressure (especially in the

standing position in some patients). RO 4 1038 was discontinued in many cases because of side effects: trembling, dizziness, constipation, paresis of the bladder, euphoria, etc. While some improvement in mood was obtained with RO 4 1038 it was also used with sedatives to provide symptomatic relief. Results are as yet inconclusive.

[No address]

1837 Favier, M., Ramel, P., & Toffol, de M. Intérêt du Méprobamate injectable en milieu psychiatrique. [The use of injectable meprobamate in psychiatry.] Lyon Médical, 1962, No. 48, 1125-1130.

Six alcoholics, suffering delirium, etc., 4 cases of agitation, 4 psychotics, 9 patients showing neurosis or depression, and 6 cases of melancholia were treated with 100 mg i.m. injections of meprobamate q.i.d. Also meprobamate was sometimes administered orally. Imipramine [dosage unspecified] was also used in melancholic states. Results were very satisfactory in neurotics and minor or moderate depressive states, as well as in the acute manifestations of chronic alcoholism. The imipramine-meprobamate combination had some ameliorating effect on the anxiety component of melancholia. Ten percent of the cases had local sensitivity because of injection. Meprobamate was well tolerated, though rarely slight tachycardia and hypotension were noted.

Hôpital Militaire Des Genettes
Lyon, France

1838 McAllister, Donald. The effect of Librium. New Zealand Medical Journal, 1962, 61, 287. [Letter].

A 22-year-old tense, depressed girl with a 9 year history of dysmenorrhea received chlordiazepoxide [dosage unspecified] q.i.d. for 1 month. In addition to the anticipated alleviation of tension and depression, her dysmenorrhea was completely obliterated, and maintenance therapy enabled her to remain symptom

free. Subsequently, 30 dysmenorrheic patients of various ages have obtained either total or partial relief with administration of chlordiazepoxide.

[No address]

1839 Lai, G., & de Penrot, E. Le Librium dans le traitement du delirium tremens. [Librium in the treatment of delirium tremens.] Praxis, 1962, 9, 236-238.

Twenty-seven alcoholics suffering from delirium tremens were treated with chlordiazepoxide (Librium) and supportive therapy. The dosage used was 100 mg, repeated 3 times in the 1st 3 hours with a maximal daily dose of 600 mg. The preferred route of administration in severe cases was i.v. and i.m. Injection was used where agitation was somewhat attenuated. This therapy usually lasted 4-5 days, whereupon drug dosage was reduced (75-150 mg/day) and maintained for 10-15 days. Agitation is quickly suppressed, but therapy must be continued. No contraindications appeared. Excellent results were obtained but true evaluation was difficult because of lack of control in relation to spontaneous cures.

Clinique Psychiatrique Universitaire
de Lausanne
Lausanne, Switzerland

1840 Mall, G., Junnemann, H. J., Kruger, H. J., & Schwartz, H. Contribution à la thérapeutique clinique au moyen du librium. [Contribution to clinical therapy, using Librium.] Annales Médico-Psychologiques, 1962, 1, 120, 971.

Four-hundred-and-ten hospitalized psychiatric patients suffering from depression and/or anxiety were given chlordiazepoxide (Librium); 30-70 mg at the beginning, reaching up to 300 mg/day. Twenty percent of cases showed improvement by the end of 10 days. The least favorable effects, partially satisfactory, were obtained with other states of depression (nonspecific, neurotic, obsessional and compulsive, depression accompanied by organic afflictions or senile arteriosclerosis). In 55 cases, chlordiaze-

poxide was used in combination with phenothiazine derivatives and in 23 cases MAO inhibitors without untoward effects.

Clinique Neuro-psychiatrique de Landeck
Landeck, Austria

1841 Grimaldi, Richard D. Propiomazine, an adjuvant for obstetric analgesia. Anesthesia and Analgesia, 1962, 41, 487-496.

Propiomazine (15 mg i.m. to 249 patients and 30 mg i.m. to 253) was administered to 502 Negro and Puerto Rican women in labor, in addition to meperidine (50 mg i.m.) and scopolamine (0.04 mg i.m.). The initial dose was repeated at 3-4 hour intervals depending upon patient response. Pain relief was evaluated by the attending physician, and blood pressure, pulse, contractions, dilatation, descent and fetal heart rate were charted before and after drug administration. Unless more frequent observations were necessitated, hourly recordings were obtained. Satisfactory analgesia was obtained by 80% on the lower dosage schedule and 87% who received the higher dosage. In general, those who received 30 mg propiomazine were quieter and more cooperative. Among this group, however, 1 case of coma occurred as did 1 case of hypotensive crisis. Results indicate that the lower dosage of propiomazine should be administered to all initially and dosage should be increased only on the basis of individual requirements. From this study, no conclusion could be drawn as to whether propiomazine in combination with meperidine is less hazardous than meperidine alone. A controlled double-blind evaluation of meperidine in combination with propiomazine, meperidine alone and morphine alone will be undertaken.

Department of Obstetrics and Gynecology
New York Medical College
Metropolitan Medical Center
New York, N. Y.

1842 Kammerer, Th., Geissmann, P., Wartel, R., & Lévy. Etude clinique,

biologique et électroencéphalographique de l'action du KT 5 (Keithon) dans certains syndromes psychiatriques. [Clinical, biological and electroencephalographic study of the action of KT 5 (Keithon) in some psychiatric syndromes.] Annales Médico-Psychologiques, 1962, 120, 119-130.

Thirty patients (8 psychotic, 7 psychoneurotic, 10 depressive neurosis with asthenia and 5 behavioral disorder) were treated with progressively increasing doses of phenoethamine (KT 5; 50 up to 300 mg t.i.d.). Four out of 8 psychotics, 5 out of 7 psychoneurotics, 6 out of 10 cases of depression and 4 out of 5 cases of behavioral disorder improved. Side effects were highly variable. Drowsiness and fine tremor (10-12 CPS) were prominent. Extrapyramidal reactions appeared during the 1st days of treatment when encountered. EEG's taken on 21 patients showed some slowing in alpha wave frequency with the appearance of slow beta and delta waves. Phenoxethamine is considered useful for its anxiolytic properties.

[No address]

1843 Pignataro, Frank P. Experience with chemotherapy in refractory psychiatric disorders. American Journal of Psychiatry, 1962, 119, 577-579.

Diazepam (10 mg b.i.d. or t.i.d. initially, then 5-10 mg/day for maintenance) was administered to 67 patients (16 schizophrenics, 9 with various psychoses and 42 psychoneurotics) with refractory illnesses for 11 months, 14 of whom received isocarboxazid (5-10 mg/day) concomitantly to combat severe depression. Laboratory tests were performed on 32 patients. A good to excellent response was obtained in 70% of all patients, 48% of psychotics and 83% of psychoneurotics, with extensive amelioration of symptoms. Combination therapy relieved all 14 depressed patients, achieving good to excellent results in 12. Good to excellent results were obtained in 7 out of 13 depressed patients treated only with diazepam. Laboratory results were well within normal limits. Side effects, although infrequent, included drowsiness,

slight transient ataxia, skin rash and stiffness of the jaw muscles. Diazepam effectively exerted a strong sedative effect without clouding the sensorium.

Psychiatric consultant
Monmouth Medical Center
Long Branch, N.J.

1844 Fish, Charles H. Use of appetite-suppressant drugs for weight reduction without dieting. *Clinical Medicine*, 1962, 69, 427-430.

A double-blind study was made on mentally retarded patients in order to observe the effects of amphetamine, dexamphetamine or no medication on the weight change. Twenty-eight patients given amphetamine lost an average of 3.8 pounds, 25 taking dexamphetamine lost an average of 3.5 pounds and 243 controls gained an average of 1.8 pounds, over a 3-6 month period. Adverse side effects were negligible. On amphetamine, additional favorable effects were reduction of high blood pressure in some cases, improvement in Fröhlich's syndrome and improvement in behavior in some. On dexamphetamine, favorable effects were noted in stutterers and in the speech of cerebral palsy patients. Also some patients gained over 10 pounds on dexamphetamine; closer examination revealed that these patients were homosexuals. They were not included in the results given above.

Fairview State Hospital
Department of Mental Hygiene
State of California
Costa Mesa, Calif.

1845 Hubata, J.A. & Hecht, R.A. Review of clinical use of hydroxyphenamate in 1759 patients. *Clinical Medicine*, 1962, 60, 1594-1598.

A group of 62 investigators used hydroxyphenamate (200 mg tablets t.i.d. or q.i.d.) in 1759 cases of somatic illness. Results were largely judged on clinical opinion, but there were 3 double-blind studies involving 95 patients. Also in another study cessation of therapy was

used as a further criterion in evaluation. The 4 categories associated with tension-anxiety which had the most patients were 422 dermatologic, 383 anxiety-tension and neurosis, 198 cardiovascular and 124 menopausal. Seventy-nine percent of patients experienced good to excellent relief. Side effects in 6% were minimal in all cases. Mild drowsiness occurred in 55, dizziness in 17, fatigue in 11, and gastrointestinal upset.

[No address]

1846 Wentzler, J. Donald. Triflupromazine (Vesprin) as an adjunct to block anesthesia. Contributory effects of single low-dosage injections. *Anesthesia and Analgesia*, 1962, 41, 301-306.

Triflupromazine (Vesprin, 3-4 mg i.v.) was administered to 84 patients, aged 19-70 years, as an adjunct to block anesthesia during 87 surgical and diagnostic procedures. Premedication initiated 2 hours before surgery included: Morphine 1/6 grain, pentobarbital 1 1/2 to 2 grains, and scopolamine 1/150 grain. In 80% of the patients triflupromazine enhanced sedation and obviated further narcotization or supplemental use of general anesthesia. Sedation level was excellent during 7 procedures, good during 64 and fair during 7. Degree of sedation was poor in 9 operations. Patients were readily placated with triflupromazine and were more inclined to accept the block procedures. There were fewer complaints of pain and awareness of the operative procedure. No untoward reactions of any consequence were encountered. One patient had a fall in blood pressure of 20 mm of mercury but no active intervention was necessary and a normal level was reestablished. Thanks to the potent antiemetic properties of triflupromazine, there were no emetic reactions. Triflupromazine is useful as a surgical premedicant in combination with traditional barbiturate-narcotic preanesthetic agents since it greatly enhances sedation.

[No address]

Clinical Studies
Abstracts 1847-1850

1847 Sherline, D. M., & Roddick J. W. Jr. A comparison of two narcotics, numporphan and emerol, in obstetrics, by double-blind technique. *Quarterly Bulletin of Northwestern University Medical School*, 1962, 36, 54-56.

In a double-blind study, 62 pregnant women in labor received numorphan (0.75 mg i.m.) and 62 received meperidine (100 mg i.m.) in conjunction with scopolamine or atropine (0.4 mg) to ascertain efficacy of obstetrical analgesia. Patients were evaluated subjectively for relief of pain, and infants were evaluated on 5 parameters of the Apgar Rating. Results of maternal analgesia indicated that 72% of the numorphan treated patients and 67% of the meperidine group experienced satisfactory analgesia. Decrease in fear and apprehension without depression was difficult to assess, but no patient was unduly depressed. No significant statistical differences were observed for maternal analgesia ratings or infant Apgar Ratings. No correlation was observed between lower Apgar Ratings and the time from medication to delivery with either of the drugs used.

Department of Obstetrics and Gynecology
Northwestern University Medical School
Evanston, Ill.

1848 Hackstein, F.G. Die Behandlung der eneehetischen Wesensänderung mit Chlorphenazine. [The treatment of epileptic personality changes with chlorphenazine.] *Medicina Experimentalis*, 1962, 6, 265-273.

Fourteen patients with severe epileptic character disturbances were treated with chlorphenazine (8 mg b.i.d.). Nine showed clear improvement in social behavior. Symptoms such as irritability, self assertiveness, awkwardness, etc. were favorably affected, however neither the character disorder per se or individual symptoms peculiar to each case were remedied. Rorschach and Behn-Rorschach tests were used in evaluation.

Rheinisches Landeskrankenhaus Suchteln
Krefeld, Germany

1849 Baron, Seymour H., & Fische, Seymour. Use of psychotropic drug prescriptions in a prepaid group practice plan. *Public Health Relations*, 1962, 77, 871-881.

In 132 working days, nonpsychiatric physicians in the Group Health Association (GHA) of Washington, D. C., wrote 1,072 prescriptions for psychotropic drugs, of which 3/4 were for psycholeptics and 1/4 was for psychoanaleptic agents (antidepressants). Tranquilizers accounted for 3% of all the prescriptions written and filled at the GHA pharmacy during the study period. Far more psychotropic drugs, particularly the amphetamines, were prescribed for females than for males. Psychotropic agents were prescribed infrequently for patients under 19 or over 70 years of age. Meproamate ranked 1st in the 40-69 age group, but dropped in rank in the 40 and under category. Psychotropic agents were frequently prescribed for the treatment of nonpsychological symptoms. Median drug dosages appeared comparable to those prescribed elsewhere by other nonpsychiatric physicians. Commonly prescribed psycholeptics included meproamate, promethazine, prochlorperazine, reserpine and rescinnamine, etc., while psychoanaleptics included the amphetamines, methylphenidate and iproniazid.

Psychopharmacology Service Center
NIMH
Bethesda, Md.

1850 Lamphier, Timothy A. Evaluation of chlormezanone as a clinical and postoperative central relaxant and tranquilizer. *Clinical Medicine*, 1962, 69, 109-111.

Eighty-three ambulatory patients, aged 13-72 years, with diversified musculoskeletal complaints received chlormezanone (100-200 mg/day t.i.d. or q.i.d.). Response to therapy was excellent in 66%, good in 20%, fair in 10% and poor in 4%. Side effects occurred in 11 cases, consisting of dizziness, nausea, weakness, rash and flushing, all of which were alleviated by a reduction in drug dosage. Therapy was discontinued in only 1 patient due to side effects. Chlormezanone safely and effectively ameliorated a variety of musculoskeletal conditions.

[No address]

1851 Beley, A., Girard, L., Leroy, C., & Pinel, J.P. L'étude de l'action du N-benzyl-beta-chloropropionamide dans les troubles caractériels de l'enfant. [The study of N-benzyl-β-chloropropionamide action in behavioral disorders of children.] *Annales Médico-Psychologiques*, 1962, 1, 120, 975.

Beclamide [dosage unspecified] was administered to children with behavioral problems. On the whole the agent was efficacious in controlling impulsiveness and instability in nonepileptic subjects who had slightly slow, dysrhythmic EEG's. Its best action was related to the improvement of predominantly neurological instability. Clinical improvement paralleled EEG improvement, i.e., diminution of slow dysrhythmia

[No address]

1852 Mandell, Arnold J., Markham, Charles H., Tallman, Frank F., & Mandell, Mary P. Motivation and ability to move. *American Journal of Psychiatry*, 1962, 119, 544-549; discussion, 549.

In a double-blind study the relationship between akinetic and rigid neurological features of Parkinson's disease, and mood state was examined. Imipramine or placebo was administered to 42 patients with Parkinson's disease. For the first week 100 mg/day was administered, followed by 150 mg in the second week and 200-250 mg for the third week. They were given the MMPI, Leary Interpersonal check list for psychological evaluation, a physical therapy check list of 106 items (self-care, etc.) and neurological examinations, as well as psychiatric examinations for the assessment of subjective mood. These patients appeared more depressed than normal, and a relationship exists between the amount of apparent subjective depression and the patient's ability to function neurologically. Tremor tended to be characteristic of the least debilitated patients, while akinesia and rigidity were linked to the most depressed, least mobile, poorly functioning group. The latter group was most aided by imipramine; here 8 out of 9 patients showed

the highest degree of improvement. While placebo effects paralleled that of the drug generally, imipramine proved superior to placebo, especially in relation to the suppression of neurological symptoms. In the discussion L. B. Kalinowsky commented favorably on the value of antidepressants in atypical depression concerning the removal of depression with concomitant improvement in neurological function.

[No address]

1853 Ollendorff, R.H.V. A trial of thioridazine (Melleril) in the maintenance of chronic schizophrenics. *British Journal of Clinical Practice*, 1962, 16, 183-186.

Thioridazine, 150 mg t.i.d., was administered to 49 chronic schizophrenics, most in partial remission, as maintenance therapy. They had been treated for the past year with high dosage chlorpromazine. There were 17 female and 32 male patients. Before thioridazine was substituted females were generally maintained on a triad of medicines - 100-200 mg chlorpromazine, 5-15 mg trifluoperazine and 50-100 mg orphenadrine, all t.i.d. Two-and-one-half to 3 months treatment was considered optimal. Forevaluation, Baker and Thorpe's interview method for deteriorated schizophrenics was employed. Marked improvement was observed in 2 patients, no change in 16 and degrees of deterioration in 31. Thioridazine was found less potent than the original medications but its use is advocated, where possible, because of its lesser side effects. Thioridazine should be tried in chronic, catatonic and hebephrenic cases with periodic remissions, particularly where tension is marked.

St. Augustine's Hospital
Chartham Downs
Canterbury, Kent
Great Britain

1854 Brown, R. W. Barr, Hamilton-Hislop, H. G., & Pritchard, J. G. A comparative clinical trial in the elderly of Distaval. *British Journal of Clinical Practice*, 1962, 16, 643-648.

Clinical Studies
Abstracts 1855-1857

Thalidomide (Distaval; 100 mg), glutethimide (Doriden; 500 mg) and Welldorm (chloral hydrate and phenazone; 1300 mg) were administered to 74 elderly patients, most 70-89 years of age, in order to determine which drug is the most useful in the management of insomnia. Observations were made on 36 nights; each drug administration was varied by means of a Latin square design in order to insure that all possible sequences were used. All drugs produced good sleep on most nights: 84.7% for thalidomide, 83.8% for Welldorm and 76.4% for glutethimide. No toxic or cumulative effects were noted, except that the incident of occasional hangover was greater for glutethimide.

Geriatric Unit
Queen's Hospital
Croydon, Surrey
Great Britain

1855 Gutiérrez Agramonte, E. El tratamiento preventivo de las depresiones con el Tofranil. [Preventive treatment of depression with Tofranil.] Revista Cubana de Medicina, 1962, 1, 110-112.

Eighteen depressed patients were given maintenance doses of 25-100 mg imipramine (Tofranil). Another group of 13 received 50-200 mg/day imipramine. Thirteen of the patients received 200-400 mg/day chlorpromazine concomitantly. The group receiving the higher dosage of imipramine were successfully maintained. This was also true for the 14 patients who received chlorpromazine-imipramine. The combined treatment is favored.

Psiquiatra Servicio
Hospital de Dementes
Havana, Cuba

1856 Gutiérrez Agramonte, Edmundo. Evolución histórica del tratamiento de la psicosis maniaco depresiva. [The historical development of treatment of manic depressive psychosis.] Revista Cubana de Medicina, 1962, 1, 78-84.

In a historical exposition of therapy for manic depression, the complementary roles of psychotherapy and chemotherapy are detailed. The high-dosage i.m. use of phenothiazine derivatives and/or ECT, as well as MAO inhibitors is advocated. Emphasis is placed on the value of imipramine. One-hundred-and-fifty depressed patients were treated with imipramine i.m. [dosage unspecified] or given 200 mg oral doses. In endogenous depression 68% recovered and in delusional melancholia 59%. Four additional cases of depression were completely cured.

Hospital Nacional de Dementes
Havana, Cuba

1857 Nussbaum, Harvey E. A new psychotherapeutic-anticholinergic combination for gastrointestinal disorders. American Journal of Gastroenterology, 1962, 38, 575-582.

Chlordiazepoxide combined with clidinium bromide (Librax) was studied for 12 months with 97 patients having symptoms referable to the gastrointestinal tract, and in whom anxiety was more or less prominent. Fifty were diagnosed as having gastrointestinal neurosis without evidence of organic disease, while the rest had somatic disorders, e.g., 8 with active duodenal ulcers. Several dosages were tried and the optimal dosage was concluded to be 1 capsule (5 mg chlordiazepoxide and 2.5 mg clidinium bromide) t.i.d. Other medications were also given, such as insulin in diabetic cases. In gastrointestinal neurosis improvement was marked in 30, moderate in 15, minimal in 3 and unchanged in 2; for the total caseload of 97 improvements were *ibid.*, 56, 29, 5 and 7. For the target symptom anxiety present in all the patients, results were, *ibid.*, 56, 29, 5, and 7. Nine patients complained of 1 or more side effects. These consisted of drowsiness in 3, dry mouth 7, forgetfulness 1, blurred vision 1, and hoarseness 1. Drowsiness in the 3 patients was sufficiently severe to necessitate discontinuation of the drug. Of 3 patients receiving placebo and active drug alternately

and double-blind, improvement occurred
with the drug and symptoms returned
on placebo.

See also 1726, 1728, 1752, 1759, 1948

[No address]

SIDE EFFECTS

1858 Schlake, Friedrich. Über den blutdrucksenkenden Effekt moderner Psychopharmaka und seine therapeutische Beeinflussbarkeit durch das Kreislaufmittel Novadral. [The hypotensive effect of modern psychotropic drugs and its management by means of the analeptic drug Novadral.] Münchener Medizinische Wochenschrift, 1962, 104, 555-557.

Studies of the blood pressure in 67 psychiatric patients under treatment with psychotropic drugs (phenothiazines and MAO inhibitors, not further specified) showed hypotensive effects in 36 cases, particularly in those with initial hypotension or given higher doses of the drugs. This side effect was successfully controlled by administration of m-hydroxyphenylethanolamine (Novadral) in doses varying from 15-40 drops t.i.d. p.o. with oral psychotropic drugs to 1 ampule b.i.d.-t.i.d. parenterally with parenteral psychotropic drugs or high oral doses. Two case reports are included, 1 of which showed that control of the hypotension may be accompanied by improvement in mood.

Nervenlinik Morija
Anstalt Bethel bei Bielefeld
Bielefeld, Germany

1859 Lenz, W., & Knapp, K. Thalidomide Embryopathy. Archives of Environmental Health, 1962, 5, 100-105.

One-hundred-and-twenty-nine reports of abnormal infants were collected in Hamburg and environs. In 90 cases there was convincing evidence of thalidomide intake in early pregnancy. An additional 203 cases were reported to the authors by letters from West Germany and abroad; parents or doctors usually wrote because the mothers had taken thalidomide. Types of malformations are discussed in an attempt to determine the critical period for embryopathy. Thalidomide intake between the 27th and 30th day after conception will affect the arms, and later intake damages the legs and to a lesser degree the arms.

Universitäts-Kinderklinik und Poliklinik
Martinistrasse 52,
Universitäts-Krankenhaus Eppendorf
Hamburg 20, Germany

1860 Grimlund, K. Fenacetinmissbruk i en svensk industri. [Phenacetin abuse in Swedish industry.] Nordisk Medicin, 1962, 67, 756.

One Swedish city, unspecified, had an incidence of phenacetin abuse 5-10 times higher than any other Swedish industrial town. Out of 200 phenacetin abusers, 34% had kidney damage while 700 nonusers showed an incidence of kidney damage of 2.5%. The number of deaths due to renal insufficiency has also shown a marked increase in the last 3 decades. Phenacetin had been ingested with the hope of increasing work capacity and not of suppressing pain.

[No address]

1861 Ringertz, N. Patologisk-anatomisk fynd i njurarna vid fenacetinmissbruk. [Pathological findings in the kidney in phenacetin abuse.] Nordisk Medicin, 1962, 67, 755.

At autopsy, a constant finding was chronic interstitial inflammation with atrophy of the kidney in persons habituated to phenacetin. Necrosis of the papillae without signs of myelitis is a common finding.

[No address]

1862 Ruikka, Ilmari, & Sourander, Leif B. Fenacetinmissbruk och njurfunktion i ett geriatriskt material. [Phenacetin abuse and kidney function in geriatrics.] Nordisk Medicin, 1962, 67, 756.

Two-hundred patients over 60 years of age (average age 75) had kidney dysfunction and pyelonephritis due to phenacetin abuse. Daily abuse was common and frequently of long standing. Pyelonephritis was more common in phenacetin users than in other patients. No significant differences could be found from normal in the plasma creatinine, the phenol red test and hemoglobin.

[No address]

1863 Tewes, H. Vitamintherapie der Contergan-Neuritis. [Vitamin therapy in neuritis due to thalidomide.] Münchener Medizinische Wochenschrift, 1962, 104, 269.

Favorable experience with combinations of vitamin B₁ (100 mg) and B₁₂ (300 µg) is noted in several cases of neuritis due to thalidomide (Contergan). The vitamins are administered parenterally at 10-day intervals.

Frueaufstrass 1
Passau-St. Anton, Germany

1864 Degkwitz, Rudolf, & Nesswetha, Lieselotte. Zwischenfall bei kombinierter Verwendung von einem Phenothiazinderivat und einem Monoaminoxidasehemmer. [Complications due to combined administration of a phenothiazine derivative and a monoaminoxidase inhibitor.] Nervenarzt, 1962, 33, 138-139.

Severe confusion, catatonia developing into extreme restlessness and sympathicotonic symptoms (tachycardia, hypertension, pupillary dilation, positive Babinski) lasting approximately 5 hours were observed in a 38-year-old woman following 17 days' treatment for manic-depressive depression with phenelzine (1 tablet 4-6 times a day) plus perazine (50 mg 3-4 times a day); this therapy had been begun 2 days after successful treatment with imipramine (250 mg/day for about 3 weeks). The sympathicotonic crisis responded to treatment with barbiturates, but the combination of imipramine with MAO inhibitors is strongly contraindicated.

Universitäts-Nervenklinik
Frankfurt am Main, Germany

1865 Quirós Corujo, Pedro G., & Rodríguez Martínez-Sierra, Gabriel. A propósito de un caso de intento de suicidio con el tofranil. [On a case of attempted suicide with Tofranil.] Actas Luso-Españolas de Neurologia y Psiquiatría, 1962, 21, 165-172.

After discussion of the pharmacological properties of imipramine (Tofranil) including its clinical use with and without other anxiolytic agents, a case of a 30-year-old depressed woman treated with imipramine

and psychotherapy is detailed. She took 50 25/mg tablets of imipramine in a suicide attempt. She became confused, drowsy and anxious. Intense headache, nausea, loss of equilibrium, a tachycardia of 97, mydriasis, lack of visual accommodation with visual blurring and diplopia, dry mouth and skin, etc. were evident. Treatment consisted of gastric lavage with an aqueous suspension of charcoal and then hypertonic magnesium sulfate was administered every 6 hours. Additionally 6-methyl prednisolone was administered every 12 hours. The patient recovered uneventfully.

Hospital Psiquiátrico Provincial de Oviedo
Oviedo, Spain

1866 Hopkins, Paul, & Robertson, Duncan. The effect of "Ancolan" and other drugs in early pregnancy. Medical Journal of Australia, 1962, No. 9, 329-330. [Letter]

Meclozine (Ancolan) and Ancoloxin (meclozine and pyridoxine) were administered to 200 pregnant women prior to the 16th week of pregnancy. Of the 200, 125 received meclozine and 75 received Ancoloxin; 187 had normal children, 8 babies were stillborn and 5 evinced various fetal anomalies. The incidence of anomalies was approximately normal, and, no correlation could be detected with respect to the nature of the defects. Apparently, meclozine and Ancoloxin may be safely administered to women during pregnancy.

Brisbane and Gordon Street
Mackay, Queensland
Australia

1867 Woodyatt, P. B. Thalidomide. Lancet, 1962, No. 7232, 750. [Letter]

A 68-year-old woman with an extensive X-ray resistant mixed mesodermal endometrioma received thalidomide (400 mg t. i. d.) for 8 days to investigate potential anticarcinogenic drug effects. The patient remained rather sleepy, and the tumor apparently underwent a slight increase in size. Therapy was maintained for another week. Further trials to determine the cytotoxicity of thalidomide in

Side Effects
Abstracts 1868-1872

malignant disease are contemplated.

Hammersmith Hospital
London, W. 12, Great Britain

1868 Wigglesworth, Robert. Thalidomide-damaged infants. *Lancet*, 1962, No. 7251, 349. [Letter]

A 5 1/2-year-old girl afflicted with quadrilateral micromelia was readily accepted by her parents and family once the initial shock of her disability had been dissipated. Regular limb-fittings facilitated the development of grasping and walking skills at periods which were optimal psychologically. The child evidenced remarkable prowess in adjusting to and utilizing her prosthetic devices. Medical and financial support coupled with parental encouragement were important factors in contributing to this child's wellbeing and societal acceptance, including attendance in regular public schools rather than a school for the physically handicapped. Obviously, the initial step in dealing with thalidomide-damaged children who manifest similar disabilities involves the development of an understanding and cooperative parental attitude.

Kettering, Northamptonshire
Great Britain

1869 Taylor, S. W. Thalidomide in pregnancy. *New Zealand Medical Journal*, 1962, 61, 423.

A male child with typical congenital malformations was born to a woman who had ingested thalidomide, 100 mg/day, from the 4th to the 8th week of pregnancy. A direct correlation apparently exists between administration of thalidomide during gestation and resultant congenital anomalies.

[No address]

1870 Teitelbaum, I. Electrocardiographic changes associated with phenothiazine. *Lancet*, 1962, No. 7272, 115. [Letter]

In approximately 30% of the patients who had undergone [unspecified] phenothiazine therapy for varying periods of time, characteristic

ECG changes were observed, including low voltage in the standard leads with widening QRS complexes and a flat or isoelectric T wave, especially in the AVL lead and an inverted T in the right precordial lead. Cessation of treatment resulted in restoration of normal ECG tracings. No underlying organic aberration could be detected.

Malben Hospital
Shaar-Menasch, Israel

1871 Wright, O. L. Thalidomide. *New Zealand Medical Journal*, 1962, 61, 56.

On the basis of reports from 2 overseas sources which associate thalidomide ingestion during early pregnancy with fetal defects, the Distillers Company Biochemicals Limited, has seen fit to withdraw all products containing thalidomide from the market pending further investigation.

[No address]

1872 Melvin, K. W. W. Tetanus-like reactions to the phenothiazine drugs "the grimacing syndrome." *New Zealand Medical Journal*. 1962, 61, 90-92.

A tentative diagnosis of tetanus was tendered for 10 patients with extensive intermittent muscle spasms involving the jaw, tongue, face, neck extensors and recti abdominis, 8 of whom had recently received prochlorperazine, 1 chlorpromazine and 1 perphenazine. Initial trismus precipitated facial muscle spasms which produced a typical risus sardonicus. Representative case histories included 4 women aged 20-72 with the above symptoms (which were really deleterious side effects from the respective phenothiazines, 25 mg/day i.m. to 25 mg t.i.d. p.o.) who experienced alleviation of spastic activity within 20 minutes to 4 hours following administration of pethidine, phenobarbital, amytal or amylobarbital. Symptoms appeared within 12-48 hours after phenothiazine injection, indicating an acute reaction. Symptoms which distinguish acute phenothiazine toxicity from tetanus include the painful, variable and intermittent nature of the masseter

spasms, the ability to overcome trismus voluntarily, and the fluctuating spasm of facial muscles, platysma and tongue. The reaction persists for 4-6 hours, but may be dissipated more rapidly with barbiturates, parasympatholytic or antihistaminic drugs normally used in the treatment of parkinsonism.

Medical Registrar
Auckland Hospital
Auckland, New Zealand

1873 Dominikovich, E. G. Drug toxicity.
New Zealand Medical Journal. 1962, 61,
467-469

Imipramine (at least 14 25 mg tablets), promethazine (20 10 mg tablets) and quinine bisulphate (3 grains) were accidentally ingested by 3 children aged 17 months-4 years due to parental carelessness. Within 4 hours after imipramine ingestion, examination revealed deep unconsciousness with Cheyne-Stokes respiration, an imperceptible heart beat, unrecordable blood pressure, central and peripheral cyanosis and extremely cold extremities. Administration of coramine, prostigmine and aramine failed to prevent death. Promethazine produced tetanic convulsions with respiratory complications 2 hours after drug ingestion. Discovery of a drug overdose was followed by gastric lavage, but death ensued due to respiratory failure some 3 hours later. An overdose of quinine tablets resulted in pallor, a semi-comatose state, hypotonicity and shallow respiration. Administration of coramine and prostigmine followed by gastric lavage resulted in recovery but failed to substantially ameliorate drug-induced retinal defects. An outline designed to preclude or diminish further instances of accidental drug overdosage offers detailed suggestions for the role of the government, the physician, parents and drug companies.

Waikato Hospital
Hamilton, New Zealand

1874 Jorgensen, Finn. Psykose udlost af metylfenidat. [Psychosis produced by methylphenidate.] Nordisk Medicin, 1962, 67, 379-380.

A 28-year-old retarded woman overused methylphenidate by giving herself i. v. doses up to a level of 600 mg/day for about 5 months at which time she was admitted to a state hospital. The patient showed paranoid symptoms after 14 days of methylphenidate abuse. In the week before admission she hallucinated. The patient recovered without withdrawal symptoms and was released after 5 days. The symptoms of methylphenidate psychosis are similar to those of amphetamine psychosis.

[No address]

1875 Hangaard, Gunnar. Iproniazid som arsak til hepatocellulaer icterus. [Hepatocellular icterus caused by iproniazid.] Nordisk Medicin, 1962, 68, 1071-1073.

A 38-year-old woman, treated for depression, ingested a total of 175 tablets of iproniazid with a maximum daily dose of 150 mg. She suffered icterus, nausea and pain, as well as pruritis. The clinical and laboratory picture indicated hepatocellular disease. While it has not been established that iproniazid has caused such damage care should be taken in the use of the drug.

Menighetssosterhjemmets Klinik
Oslo, Norway

1876 Ahlberg, Ake. Decubitalsor efter suicidalforsök. [Decubital ulcers following suicide attempts]. Nordisk Medicin, 1962, 67, 376-377.

Case reports were presented for 6 cases suffering from decubital ulcers following recuperation from various suicide attempts. In 1 case an unknown number of tablets of meprobamate, prothipental, mebymal and chlorpromazine had been ingested. The patient was discovered unconscious and it was impossible to discern the time factors involved. On admission he had sores over the sacrum, heels and occipital regions. These cases were treated with plastic surgery.

Plastikkirurgiska Kliniken
Malmö, Sweden

Side Effects
Abstracts 1877-1880

1877 Hallwright, G.P. Agranulocytosis with alpha methyl dopa. New Zealand Medical Journal, 1962, 61, 470-472. [Letter]

Agranulocytosis in a woman [age unspecified] secondary to α -methyl-dopa (102 g) administration over a period of 18 weeks was ameliorated upon drug discontinuation. Stabilization of the blood picture was obtained with guanethidine (10 mg) combined with hydrochlorothiazide. As a trial measure, a specially purified preparation of α -methyl-dopa (2.75 g) was subsequently administered over a period of 16 days. Blood counts were monitored constantly. No untoward subjective reactions occurred, other than hypotension when a single 750 mg dose was ingested rather than the usual divided dose. Since no drug hypersensitivity was observed, the previous agranulocytosis could have been due to the presence of trace amounts of an impurity such as D- α -methyl-dopa or ammonium chloride. To preclude the possibility of an endogenous change in reactivity, purified α -methyl-dopa (total dose 6, 250 mg) plus hydrochlorothiazide (25 mg/day) were administered for 12 days, after which a slight neutropenia was observed which persisted for 2 weeks after drug discontinuation. No true hypersensitivity was manifested, but the discomfort and inconvenience attendant upon continual blood studies precipitated a return to guanethidine.

Hypertension Clinic
Wellington Hospital
Wellington, New Zealand

1878 Bargues, R., Planques, L., Cohadon, S., & Loiseau, P. A propos d'une série récente d'accidents nerveux dus aux hydantoïnes. [On a series of recent nervous accidents due to hydantoins.] Annales Médico-Psychologiques, 1962, 1, 120, 968-969.

Twenty cases of intoxication caused by N-3-methyl-5,5-diphenylhydantoin are reported. However, the supposition is put forth that the toxicity was due to impurities accidentally incorporated at manufacture. Acute cerebello-labyrinth syndrome, regressing several days after cessation of

drug therapy, subacute encephalopathy for 3 months after cessation of medication, and clinical signs disappearing in 1-2 days were cited. EEG's showed significant anomalies: slowing in alpha rhythm, frequent slowing in fundamental activity (delta activity permanently diffuse) and other signs.

[No address]

1879 Pihkanen, T., & Harenko, A. Bromisovalum intoxication: its differential diagnosis from neurological disorders. Acta Neurologica Scandinavica, 1962, 38, 209-216.

The toxicity of bromisovalum is mainly due to the bromine effect, but in part the compound in itself has toxic effects with the consequence that symptoms appear with lower bromine content than in bromine intoxication. The symptoms are the same as those of bromism in general: psychic disturbance, ataxic symptoms, reflex changes, sensory disturbances and other neurological signs. Six illustrative cases are given.

II Department
Hesperia Hospital
Helsinki, Finland

1880 Gayral, L., Robert, P., Bardis, Cl., & Turnin, J. Crises oculogyres du syndrome dyskinétique des médicaments neuroleptiques. [Oculogyric crises in neuroleptic-induced dyskinetic syndrome.] Annales Médico-Psychologiques, 1962, 1, 120, 303. [Abstract]

Twenty-four cases of oculogyric dyskinetic crises caused by chlorpromazine, thio-properazine, haloperidol, prochlorperazine, fluphenazine and reserpine were studied. The crises appeared generally at the start of treatment. They were often accompanied by cervico-brachio-lingual dyskinesia, neuro-autonomic signs and anxiety, agitation and depression. Treatment and prevention similar to that given for the oculogyric crises of epidemic encephalitis are suggested.

[No address]

1881 Uhrbrandt, Lisbeth, & Faurbye, A. Cerebral dyskinesi ved medikamentel behandling af psykoser. [Cerebral dyskinesia during the medical treatment of psychosis.] *Nordisk Medicin*, 1962, 67, 389-390.

Among 29 patients suffering from dyskinesia syndrome, 15 had been treated with perphenazine, 10 with chlorpromazine and 1 with reserpine [dosages unspecified]. In 12 patients the medication was continued but in 2 of these the symptoms disappeared after dosage reduction. In 17 the treatment was interrupted and 11 of these showed irreversible dyskinesia throughout an observation period of 4-22 months. At a later examination it was found that dyskinesia had disappeared in 1 of these cases after 6-7 months. Three other drug-induced (thioridazine) cases of dyskinesia were observed; 1 of these remained dyskinetic even after 3 1/2 months. Drug-induced dyskinesia usually appeared in elderly patients and in those suffering from organic disease with long-term therapy.

[No address]

1882 Max, Paul, & Hobbs, G.E. Addiction and tranquilizers. *Medical Services Journal, Canada*, 1962, 18, 431-434.

A 37-year-old woman with muscular dystrophy and a previous history of secobarbital addiction received meprobamate [dosage unspecified] to combat overt anxiety, and was soon taking 10 400 mg tablets of meprobamate per day. Admission revealed a restless, anxious and agitated patient who was ataxic and unable to walk without support. Administration of meprobamate (400 mg) was followed by a grand mal seizure. Drug withdrawal was accomplished over a 2-week period, with chloral hydrate as the only sedation. The EEG was within normal limits, and the patient was discharged 1 month after admission on chloral hydrate and chlorpromazine [dosage unspecified]. She was free of any medication within a few months. Evidence culled from the literature indicates that meprobamate is not a primary addicting drug per se, but withdrawal symptoms and psychic dependency are sometimes observed in patients so predisposed.

Westminster Hospital
London, Ontario
Canada

1883 Weir, D.G., & Carson, J.F. A further fatal case of Doriden intoxication. *Irish Journal of Medical Science*, 1962, No. 433, 20-22.

A 64-year-old chronically depressed woman was admitted unconscious with pupils dilated; corneal and gag reflexes were absent and the fundi were normal; all reflexes were very sluggish and no positive Babinski sign, after apparently ingesting 25 g glutethimide (Doriden). In the 5 hours after admission respiration rate fell but this was corrected by 2 ml 5% vanillic acid diethylamide i.v. given hourly and then 5 ml i.m. 6-hourly. Standard gastric lavage and prophylactic antibiotic therapy were given. Some 21 hours later the blood pressure had fallen to 80/40 and continued to fall in spite of i.m. amphetamine. Some 6 hours later she died.

School of Medicine
Trinity College
Dublin, Ireland

1884 Pretto, John I. Observations on the effects of a narcotic, including accidental overdose. *Clinical Medicine*, 1962, 69, 2011-2013.

An overdose of piminodine (300 mg p.o. within 2-4 hours) was taken by 2 men 52 and 66 years of age, who were members of a group of 42 patients receiving the drug in conjunction with x-ray therapy for cancer. Both men rapidly developed tachycardia and tachypnea, with diminution of peripheral pain sensation but no disturbance of mental alertness, intellect or consciousness. Nausea and vomiting occurred in 1 patient. Following ingestion of the standard dose of piminodine (50 mg p.o. every 4 hours), another patient showed allergic urticaria which was promptly alleviated by parenteral antihistamine. Piminodine seems able to produce analgesia without causing euphoria or narcosis.

Department of Radiology
College of Medicine
University of Illinois
Chicago, Ill.

Side Effects
Abstracts 1885-1888

1885 Benitz, K.-F., Moraski, R., Roepke, R.R., & Wozniak, Lillian A. Toxicity studies on mephenoxalone in rats and dogs. *Toxicology and Applied Pharmacology*, 1962, 4, 220-237.

Toxicity data for mephenoxalone after oral administration to beagle dogs (1-month and 6-month studies) and Sherman rats (1-month study) are reported. In the dog, daily doses of 480 and 600 mg/kg administered for 3-4 weeks produced toxic effects such as anorexia, loss of body weight, ataxia, hemolytic anemia, etc. Slight hemolytic anemia was detected in the dogs on 200 mg/kg for 1 month. No toxicity was observed with daily doses as high as 120 mg/kg for a period of 6 months. Daily oral doses of approximately 1000 mg/kg for 30 days to rats produced decreased food intake and body weight gain. Slight decrease in body weight gain was observed in the female rats receiving 280 mg/kg. Daily doses of 70 mg/kg for 1 month were well tolerated.

Lederle Laboratories Division
American Cyanamid Company
Pearl River, N. Y.

1886 Algeri, Elvera J., Katsas, George G., & Luongo, Michael A. Determination of ethchlorvynol in biologic mediums, and report of two fatal cases. *American Journal of Clinical Pathology*, 1962, 38, 125-130.

Two suicides (ingestion of unknown amounts of ethchlorvynol) prompted the establishment of a method for its determination, based on the color reaction produced in compounds with an allyl group on treatment with phloroglucinol and concentrated HCl. The procedure was applied to 7 samples of whole blood and liver. As well, blood samples from 2 healthy adults were analyzed following ingestion of 2500 mg capsules (ca. 12 mg/kg) of ethchlorvynol at 0.5 hour intervals for 2 hours, then at 3, 4, 6 and 24 hours after ingestion. The side effects produced (which disappeared 3 hours after ingestion) included: drowsiness, slurring of speech, unsteady gait, double vision and muscular incoordination. Analysis was also made of concentrations of ethchlorvynol in blood, liver and kidneys of the 2 described cases of suicide. Attempts to determine whether unchanged drug or metabolites were extracted were unsuccessful.

Department of Legal Medicine
Harvard University Medical School
Boston, Mass.

1887 Dundee, John W., McCleery, W.N.C. & McLoughlin, George. The hazard of thiopental anaesthesia in porphyria. *Anesthesia and Analgesia*, 1962, 41, 567-574.

Three women, aged 23-32 years, 2 with hematuria and 1 with an acute abdominal emergency received thiopental (350-550 mg) anesthesia, which precipitated an acute exacerbation of underlying porphyria that resulted in death in 2 patients and extensive paralysis in the 3rd. Porphyria can be divided into 3 distinct diseases: porphyria congenita, porphyria cutanea tarda and acute intermittent porphyria. Barbiturates per se do not cause acute porphyria. However, barbiturates (particularly those containing an allyl group) given for a long time to a patient with a genetic defect may precipitate an attack. A relationship between barbiturate administration during an attack of porphyria and the onset of paralysis may exist. Chlorpromazine is of value in treating pain; in severe pain meperidine, neostigmine or ganglionic blocking drugs may be efficacious for known porphyrics, all the inhalation anesthetic agents and the analgesics may be used with impunity, while barbiturates are contraindicated.

Department of Anaesthetics
Queen's University of Belfast
Belfast, Great Britain

1888 Frandsen, Emil. Toxic amblyopia during antidepressant treatment with pheniprazine (Catran). *Acta Psychiatrica Scandinavica*, 1962, 38, 1-14.

The side effects of several imino-dibenzyl derivatives and MAO inhibitors are reviewed with particular reference to visual disturbances. Five cases of visual impairment after 3-11 months treatment with pheniprazine in considerably higher than recommended dosage (for the most part, 8-24 mg daily) are reported. During pheniprazine treatment or just prior to it, all cases had received additional medication including chlorprothixene, iproniazid and meprobamate. In 2 of the patients the visual impairment was marked with mild bilateral optic atrophy and persisting visual impairment. All patients

also showed red-green colorblindness with, in all cases, centrocecal scotomas for white. In severe cases red-green perception was entirely lost. Restitution was slow in all cases. There was a similarity to tobacco-alcohol amblyopia. Upon any sign of visual impairment, MAO inhibitor therapy should be stopped or the dosage reduced.

Department of Ophthalmology
St. Hedvig Hospital
Copenhagen, Denmark

1889 Del Greco, Francesco, Arieff, Alex J., Simon, Norman M. Acute barbiturate and glutethimide intoxication. Quarterly Bulletin of the Northwestern University Medical School, 1962, 36, 306-315.

Twelve patients with acute intoxication, 8 from barbiturates (phenobarbital, secobarbital, amobarbital: 1.0-10.0 g) and 4 from glutethimide (8.5-12.5 mg) are cited. Supportive therapy was administered to 3 patients while the remaining 9 received peritoneal dialysis and hemodialysis. Degree of intoxication upon admission ranged from I-IV, and duration of coma before admission, 2-65 hours. Treatment included gastric lavage, establishment and maintenance of an adequate airway with endotracheal intubation, intermittent positive pressure respiration, analeptics (amphetamine, megride, etc.), pressor agents (levarterenol), antibiotics, fluids and nursing care. All 3 of the patients who received only supportive therapy recovered uneventfully. Two of the 3 treated with peritoneal dialysis recovered, and the 3rd died from respiratory distress and circulatory failure. The 7 subjected to hemodialysis recovered but 1 had severe residual brain damage. Hemodialysis is the most effective means for treating barbiturate and glutethimide intoxication, particularly if instituted early.

Department of Medicine
Northwestern University Medical School
Evanston, Ill.

1890 Harthorne, J.W., Marcus, A.M., & Kaye, M. Management of massive imipramine overdosage with mannitol and artificial dialysis. New England Journal of Medicine, 1962, 1, 33-36.

A 21-year-old woman addicted to barbiturates

and morphine ingested 10 100 mg tablets of Tuinal (amobarbital and secobarbital) and a large amount of whiskey the night before she swallowed 215 25 mg tablets of imipramine (5375 mg) in a suicidal attempt. Within 3 1/2 hours she was apneic and deeply comatose, with marked hypotension and absent corneal and plantar reflexes. Gastric lavage, dextran and metaraminol failed to control hypotension. Tonic-clonic seizures were relieved by amobarbital (0.25 g i.v.). Levarterenol i.v. maintained blood pressure. Dialysis on an artificial kidney for 5 1/2 hours was initially complicated by generalized convulsions and 2 episodes of cardiac arrest. Administration of mannitol (50 g i.v.) induced osmotic diuresis. The temperature of the dialysis bath was lowered to 95°F, to decrease the patients temperature from 107°F to 96°F. Levarterenol and methoxamine controlled hypotension after cessation of dialysis. Analysis of the dialysis bath water revealed only 30 mg of imipramine in 300 liters. Early recovery was characterized by myoclonic jerking and athetoid movements as well as auditory and visual hallucinations. No neurological damage was evidenced 3 months after the above episode and the ECG was normal.

Massachusetts General Hospital
Boston, Mass.

1891 Alajem, N., & Albagli, Ch. Severe imipramine poisoning in an infant. American Journal of Diseases of Children, 1962, 103, 702-705.

A 1 1/2 year old girl accidental ingested 375-500 mg imipramine and became comatose with gross neurological disturbances and severe myocardial damage with corresponding EEG and ECG changes. She was treated symptomatically with barbiturates and made a complete clinical, electroencephalographic, and electrocardiographic recovery.

"Asaf Harofe" Government Hospital
Zerifin, Israel

See also 1663, 1674, 1683, 1685, 1686, 1688, 1689, 1691, 1693, 1698, 1699, 1706, 1707, 1711, 1712, 1713, 1725, 1749, 1753, 1761, 1773, 1827, 1906, 1908, 1909, 1914, 1915, 1917, 1931, 1933, 1938, 1968, 1969

BEHAVIORAL STUDIES

1892 Ostfeld, Adrian M., & Aruguete, Alayne. Central nervous system effects of hyoscine in man. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 133-139.

A series of experiments was performed with 54 normal paid volunteers in order to assess hyoscine CNS effects (EEG and behavior). Subjects reported in the fasting state, their pupils were dilated with 10% phenylephrine and, after 10 minutes of rest, pulse rate and saliva volume were measured. A Clyde Mood Scale was completed, electrodes were applied and the room darkened for photic stimulation. EEG's were recorded during the 30 minute control period. Hyoscine hydrobromide 0.15-0.80 mg was then injected s.c. The test parameters were recorded thereafter at intervals of a half hour. A metronome tapping task (Wilker 1954) was employed as a simple measure of alertness; the Wechsler Memory Scale, the buzzer press test, the Stroop color naming test and the card-object recall test (Terman and Merrill 1937) were also employed. The Clyde Mood Scale was retaken at 1 hour and again at 4 hours after hyoscine. EEG and gross behavioral observations were continued for at least 5 hours. Hyoscine induced a moderate bradycardia and a marked decrease in salivation and in the duration of the EEG arousal response. These effects were maximal at 1-2 hours after administration, but no longer present at 4 hours. Consistent behavioral effects in EEG experiments were a decrease in spontaneous speech and movement and a significant decrease in the "Energetic" Scale of the Clyde Mood Scale. The spontaneous EEG exhibited a consistent shift toward lower amplitude of the 5-8 cycles per second activity. The alpha index significantly decreased. The depression of the EEG arousal response may be attributed to the action of hyoscine on the ascending reticular activating system which occurs independently of the action on the spontaneous EEG rhythm. The larger hyoscine dose was associated with a decrease in performance on behavioral tests. When arecoline and methacholine were employed, in doses which antagonized the peripheral effects of hyoscine, e.g., salivation, they did not antagonize hyoscine effects on behavior.

Department of Preventive Medicine
University of Illinois College of Medicine
Chicago, Ill.

1893 Collins, William E., & Poe, Robert H. Amphetamine, arousal, and human vestibular nystagmus. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 120-125.

Twelve mg racemic amphetamine or saline was administered s.c. to normal human subjects 20 minutes before trials in order to examine the effects of the clinical dose on the vestibular response under conditions of mental activity and reverie. A rotary turntable (Guedry and Kalter 1956), located in a light-proof room, was used and the subjects were seated at the center of the apparatus in a normal sitting position. A reference electrode on the forehead and an electrode taped at the outer canthus of each eye served to record horizontal components of eye movement. Two groups were used: a "naive" group which had no previous turntable or caloric stimulation experience and an "experienced" group that had been rotated many times previously under a variety of conditions. For the 1st 2 trials on each day, mental arithmetic problems (continuous division) were assigned; for the 3rd and 4th trial, the subjects were instructed to relax and daydream, keeping the eyes open. The drug produced significant increases in cardiovascular activity. However it did not affect significantly the total amount of slow-phase nystagmus induced by rotation when instructions influencing mental activity were employed. The mentally active state resulted in greater output and longer durations of nystagmus than did the relaxed state.

Civil Aeromedical Research Institute
FAA
Oklahoma City, Okla.

1894 Korman, Maurice, Knopf, Irwin J., & Leon, Robert L. Alcohol as a discriminative stimulus. A preliminary report. *Texas Reports on Biology and Medicine*, 1962, 20, 61-63.

The feasibility of teaching rats to increase their voluntary alcohol consumption through repeated trials of an instrumental conditioning type was examined using 16 male-ragout-Dawley rats, 17 days of age. Previously they had been given a choice of water and an 8% alcohol solution for a period of 5 days. All animals were placed in a drinking box with 1 tube present for 5 minutes a day, followed by 2 minutes in an intense sound stimulation box. Some rats were placed in a drinking box with only the alcohol solution available. They were then placed in the sound box without sound stimulation. On the 2nd day these animals drank water and received 2 minutes of sound stimulation. In contrast other rats had the alcohol solution paired with sound stimulation. The median alcohol ratio of the 1st group of animals rose from 14% pre-experimentally to 60 and 61% during 2 postexperimental periods of free consumption. The alcohol ratio of the latter group fell from 13% to 0. Clearly animals can learn a discriminative response to a solution of alcohol.

Department of Psychiatry
University of Texas Southwestern Medical
School
Dallas, Tex.

1895 Furgiuele, Angelo R., Kinnard, William J., & Buckley, Joseph P. Central effects of β -phenylisopropylhydrazine and iproniazid. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 356-360.

The effects of pheniprazine (β -phenylisopropylhydrazine) and iproniazid on spontaneous and forced motor activity were investigated in male Swiss-Webster mice, using spontaneous motor activity and forced motor activity (rotarod). The chronic effects of iproniazid were studied in Wistar rats, cats and dogs. There was a marked difference in the effects of pheniprazine and iproniazid on spontaneous motor activity involved. Pheniprazine produced potent stimulatory effects whereas iproniazid greatly depressed spontaneous activity. Both compounds decreased rotarod performance time. The ataxia and hindleg weakness produced by the chronic

administration of pheniprazine to rats and dogs appears to be due to a depression of spinal synaptic pathways.

Department of Pharmacology
University of Pittsburgh School of Pharmacy
Pittsburgh, Pa.

1896 Gylys, J. A., Hart, J. J. D., & Warren, M. R. Chlorphentermine, a new anorectic agent. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 365-373.

Chlorphentermine reduced food intake in rats, dogs, mice and in gold thioglucose obese mice. The oral anorectic potencies of chlorphentermine and diethylpropion in rats were about 1/5 and in dogs 1/10 that of dexamphetamine. The acute oral toxicities of these drugs were respectively 1/8 and 1/15 that of dexamphetamine. The anorectic response of chlorphentermine in rats was prolonged and without any increase of motor activity while the effects of diethylpropion and dexamphetamine were shorter and accompanied by hyperactivity. All 3 compounds caused autonomic sympathomimetic side effects at anorectic doses which produced a prolonged anorectic response. At anorectic doses chlorphentermine and dexamphetamine increased the sensitivity of rats to quinine as reflected by an increased aversion to the drinking of quinine containing milk. The locomotor activity profile of chlorphentermine as shown with mice in rotating cages was different from that seen with dexamphetamine and diethylpropion; dexamphetamine was stimulating while diethylpropion had no consistent effect. Chlorphentermine did not antagonize chlorpromazine or reserpine depression, while diethylpropion and dexamphetamine induced reversal. Chlorphentermine had no effect on body temperature in rats in contrast to the pyrexia responses caused by dexamphetamine and diethylpropion to induce increased spontaneous activity, pyrexia responses or to reverse reserpine or chlorpromazine depression.

Department of Pharmacology
Warner-Lambert Research Institute
Morris Plains, N. J.

1897 Smith, Gene M., & Beecher, Henry K. Subjective effects of heroin and morphine in normal subjects. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 47-52.

Twenty-four healthy, nonaddicted college men between 21 and 30 years of age were used as subjects. Each was given 10 mg/70 kg morphine on one occasion, 4 mg/70 kg-heroin on another and placebo on still another. The drug order was counterbalanced so that each of the 6 possibilities of ordering the 3 medications were used with 4 subjects. Subcutaneous injections were made on a double-blind basis. The most definite subjective effects (90-item check-list of Smith and Beecher 1959) of both opiates were mental clouding, mental and physical "deactivation" and "somatic" effects such as dizziness, itching, sweating, numbness, nausea and visual difficulties. The effects on responses in the emotional areas were weaker than those aforementioned but were internally consistent. Although most subjects reported unpleasant emotional effects, 2 reported pleasant ones. The effects of the 2 opiates were similar; the main differences were that the heroin effects were stronger and reached peak degrees earlier than those of morphine. Undesirable side effects were more marked with heroin than with morphine.

Anesthesia Laboratory
Harvard Medical School
Massachusetts General Hospital
Boston, Mass.

1898 Smith, Gene M., Semke, Charles W., & Beecher, Henry K. Objective evidence of mental effects of heroin, morphine and placebo in normal subjects. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 53-58.

Forty-eight nonaddicted male students, 21-32 years of age received s.c. injections of morphine (10 mg/70 kg), heroin

(4 mg/70 kg) or placebo. In 1 study 24 subjects were given morphine and saline on separate occasions and in another study 24 different subjects were given morphine, heroin and placebo, also on separate occasions - all on a double-blind basis. Each experimental day a subject was given 2 batteries of tests: the Attention, Name-Face, Hidden Figures and Oral Addition Tests in the 1st study while the Written Addition and Verbal Facility Tests were used in the 2nd study; also the Coding and Distributed Numbers Tests were used in both studies. Heroin and morphine can produce statistically significant impairment of mental performance and the impairment is primarily one of speed rather than accuracy. Heroin impairment appears earlier and is somewhat greater than that produced by morphine. Mental impairment can be demonstrated as early as 40 minutes and as late as 5 hours and 40 minutes after the administration of 10 mg/70 kg morphine.

Anesthesia Laboratory
Harvard Medical School
Massachusetts General Hospital
Boston, Mass.

1899 Alnaes, Randolph, & Aslanov, Anatoli. Imipramins fysiologiske virkning på høyere nerveaktivitet hos mennesker. [The physiological effect of imipramine on the higher nervous activity of man.] *Nordisk Medicin*, 1962, 68, 1155-1158.

Fourteen normal subjects were given a therapeutic dose (25 mg tablets) of imipramine. Conditioned avoidance responses were assayed using the correction method of Astrup (1956) and work connections in association experiments (Astrup 1955) and oral reports. Autonomic functions were measured through pulse, blood pressure and defense reaction to a shock threshold. Changes were recorded after 60, 120, 180 and 240 minutes. Imipramine had a significant inhibitory effect on abstract verbal reactions. The speed of conditioned motor reactions was reduced and the thresholds of defense reflexes to electrical stimulation increased. The maximum for these reactions was noted 2 hours after drug administration. A diphasic effect of

amipramine (both excitation and inhibition) occurred. The interaction between the cortical-subcortical effect and the physiological basis of clinical observations is discussed.

Austad sykehus
Oslo, Norway

1900 Geller, Irving, & Seifter, Joseph. The effects of mono-urethans, di-urethans and barbiturates on a punishment discrimination. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 284-288.

Punishment discrimination was conditioned in male Sprague-Dawley-Holtzman rats (ca. 4 months old at the start of the experiment) by simultaneously rewarding with food and punishing with shock all lever responses made in a Skinner box in the presence of a discriminative stimulus (tone). Intraperitoneal injections of urethane, hedonal, emylcamate, pentobarbital, phenobarbital and meprobamate were administered just before each drug session. The rats were gradually reduced to 60% of their original weight and maintained at this level by limited feedings after each experimental session. Meprobamate, diurethane, produced the maximal attenuation at a dose (120 mg/kg) which produced a minimum of side effects. The monourethanes, hedonal, emylcamate and urethane produced the least attenuation. Pentobarbital and phenobarbital produced intermediate attenuating effects upon the punishment discrimination.

Basic Medical Sciences Research Division
Wyeth Laboratories
Radnor, Pa.

1901 McGaugh, James L., & Thomson, Calvin W. Facilitation of simultaneous discrimination learning with strychnine sulphate. *Psychopharmacologia*, 1962, 3, 166-172.

Thirty-two young rats, 16 male and 16 female, half of the S_1 strain (Tryon 1940 maze-bright strain) and half of the S_3 strain (Tryon maze-dull strain) were used

in simultaneous discrimination learning. Six minutes before the start of the training trials on the discrimination problem (procedure similar to that of Thompson and Bryant 1955), 16 were given 0.33 mg/kg strychnine i.p. and 16 given saline. There was a significant difference in the number of trials to criterion; the mean for all strychnine-treated animals was 30.5 and that for controls 81.5. The overall median of strychnine-treated subjects was 13.0, while that of controls, 40.5. Females gave superior performance, possibly either due to their lighter weight or in response to shock. Further, no significant difference was noted between strains.

Department of Psychology
University of Oregon
Eugene, Ore.

1902 Hollister, Leo E., & Hartman, Alan M. Mescaline, lysergic acid diethylamide and psilocybin: comparison of clinical syndromes, effects on color perception and biochemical measures. *Comprehensive Psychiatry*, 1962, 3, 235-241.

Mescaline (5mg/kg), LSD (1 μ g/kg) and psilocybin (150 μ g/kg) were randomly administered p.o. to 20 subjects (18 received all 3 drugs), who were free from overt psychopathology, in a single-blind study. Evaluation included a questionnaire of 43 items, completed by the subjects, regarding signs and symptoms experienced with each drug. Color perception was measured by the Farnsworth-Munsell Hue Discrimination test. Various biochemical tests (total lipids, inorganic phosphate, creatinine, etc.) were also performed. Similar clinical syndromes resulted from all 3 drugs, that from mescaline being the most pronounced. Somatic manifestations predominated and psychotomimetic symptoms were uncommon except for visual hallucinations. Color perception was altered significantly only after inadequate stimuli, a fact which tends to support the hypothesis that heightened and unusual perception of colors following psychotomimetics may result from the action of normally inadequate stimuli. The urinary excretion of inorganic

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phosphate usually decreased, total circulatory eosinophils decreased and plasma FFA increased. Except for an increase in copper oxidase activity after psilocybin, all other biochemical measurements were not significantly changed. Many common mechanisms of action apparently existed.

VA Hospital
Palo Alto, Calif.

1903 Frankenhaeuser, Marianne, Myrsten, Anna-Lisa, & Järpe, Gundla. Effects of a moderate dose of alcohol on intellectual functions. *Psychopharmacologia*, 1962, 3, 344-351.

In a single-blind study, the performance of 8 healthy subjects, aged 20-27 years, was examined in 4 tests of intelligence (verbal, numerical, inductive and spatial) following an oral dose of alcohol (0.8 g/kg). In order to maintain the blood alcohol at a constant level during psychological testing, a level of about 0.1 g/kg/hour was maintained by a 5% alcohol i.v. infusion. Two test sessions a few days apart were given each subject and the testing sequence rotated so that each test was given 1st, 2nd, 3rd or 4th an equal number of times. Comparison with placebo results showed that numerical and spatial test performance was significantly impaired, whereas verbal and inductive test performance was unaffected. Performance speed was less affected than accuracy. As the affective test is considered the most complex, results do not confirm the belief that more complex tasks are those affected by alcohol.

Psychological Laboratory
University of Stockholm
Stockholm, Sweden

1904 Posluns, Donald. An analysis of chlorpromazine-induced suppression of the avoidance response. *Psychopharmacologia*, 1962, 3, 361-373.

Male Long-Evans rats were used in a conditioned avoidance experiment with or without 3 mg/kg chlorpromazine given i.p. before test phases. The avoidance response required moving from 1 end of 1 compartment in a 2-compartment box (electrified

grids) into the other compartment. Lengthening the preshock interval increased the number of CAR's made under the influence of chlorpromazine by rats which had been previously trained without drugs. Neither intensifying the electric shock, nor introducing warning signals affected the number of responses made under the drug. Chlorpromazine induces a locomotor deficit which is not attributable to sensory deficits. Chlorpromazine did not impair CAR acquisition when the drug was injected just before training sessions and omitted for the 3rd test session. The drug did not alter the efficacy of the CAR reinforcer. Chlorpromazine induced a delay in the initiation of locomotion without affecting the running time. The length of locomotor initiation delay correlated highly with an independent measure of CAR suppression. The CAR suppression was attributable to the inability to initiate locomotion under chlorpromazine, and affect of the drug's action upon some central motor function.

Department of Psychology
University of Pittsburgh
Pittsburgh 13, Pa.

1905 Wolbach, A.B., Miner, E.J., & Isbell, Harris. Comparison of psilocin with psilocybin, mescaline and LSD-25. *Psychopharmacologia*, 1962, 3, 219-223.

Ten former morphine addicts, all prisoners aged 25-33 years, received single doses of LSD (0.75-1.5 µg/kg), mescaline (2.5-50 µg/kg) or psilocybin (37.5-150 µg/kg). All drugs were administered i.m. on a single-blind basis. The following observations were made every hour for 9 hours: rectal temperature, pulse rate, respiratory rate, systolic blood pressure, pupil diameter and kneejerk thresholds. Subjects completed a questionnaire modified from Abramson et al. (1955) every hour for 8 hours. A brief mental status examination was made by the attending physician at the height of the mental reaction and on the morning following drug administration. Psilocin, LSD and mescaline caused significant increases in body temperature, systolic blood pressure and pupillary diameter and decreased the kneejerk

threshold. Subjectively all 3 drugs caused anxiety, euphoria, impaired thinking and concentration, marked alterations in sensory perception and body image, kaleidoscopic visual "pseudo hallucinations", true hallucinations and occasional loss of insight. Symptoms appeared after psilocin administration within a few minutes, were nearly at peak within 30 minutes, and had largely subsided in less than 4 hours. Peak effects from LSD occurred in 1.5 hours, and were largely dissipated within 5-6 hours.

Peak effects of mescaline occurred 2.5 hours and persisted longer than the effects of either LSD or psilocin. With peak values for pupillary dilatation, 1 μ g/kg LSD was equivalent to 45 μ g/kg psilocin, and 1 μ g/kg psilocin was equivalent to 66 μ g/kg mescaline. Nearly identical values were obtained with the data for peak pupillary response, total or peak number of answers on the questionnaire and clinical grade.

NIMH Addiction Research Center
USPHS Hospital
Lexington, Ky.

1906 Somers, G. F. Thalidomide and congenital abnormalities. *Lancet*, 1962, No. 7775, 912-913. [Letter]

Eight New Zealand rabbits received thalidomide (150 mg/kg/day p.o.) from day 8 to 16 of pregnancy. Litters produced by 3 of the rabbits contained stillbirths and young with deformities. The 4th yielded evidence of fetal autolysis. Characteristic fetal defects were observed. In a 2nd experiment involving 8 does, thalidomide administered as above induced similar malformations in the 1st 4 litters. Improved screening methods for new drugs must be instituted. Detailed results of similar experiments with mice, rats and hens' eggs will soon be published.

Distillers Co. (Biochemicals) Ltd.
Speke, Liverpool
Great Britain

1907 Feldman, Shaul. Electrophysiological alterations in adrenalectomy. Changes in brain stem conduction, excitability, and sensitivity to anesthesia in adrenalectomized cats. *Archives of Neurology*, 1962, 7, 460-470.

Chronically adrenalectomized hydrocortisone-supported cats were studied and compared with intact animals in order to study possible neurophysiological disturbances in hypoadrenalism. Blood level determinations for glucose, sodium, and chloride were made for 7 adrenalectomized cats prior to surgery. Concentric electrodes were introduced stereotaxically into the medial lemniscus, midbrain reticular formation and ventromedian and the posterolateral hypothalamic regions. At the end of surgery the cats were immobilized with gallamine triethiodid (Flaxedil) and maintained on artificial respiration. Stimuli were delivered to the contralateral sciatic nerve. The evoked potentials were recorded monopolarly in the different brain stem regions. Neuronal recovery in the medial lemniscus, the midbrain reticular formation and the hypothalamus was studied by delivering paired shocks to the sciatic nerve at varying intervals. The neuronal recovery was determined by expressing the amplitude of the response to the second

of a pair of shocks as a percentage of the amplitude of the response to the 1st of the same pair. In order to determine the effect of pentobarbital on the evoked potentials, 1 mg/kg of the drug was administered i.v. in small increments. In the multisynaptic structures of the reticular formation and the ventromedian hypothalamus of adrenalectomized cats, the latency of the evoked potentials upon sciatic nerve stimulation was prolonged, indicating slowing in CNS conduction; their neuronal recovery was delayed, and they had a greater susceptibility to pentobarbital when compared with intact animals. On the other hand, the latency and neuronal recovery of the evoked potentials in the oligosynaptic pathways of the medial lemniscus and the posterolateral hypothalamus were found to be the same in the intact and adrenalectomized cats. These findings indicate a disturbance at synaptic levels in the brain stem of adrenalectomized animals. Neurophysiological alterations relating to the adrenal cortex may be partially responsible for neurological and mental disturbances encountered in patients with hypoadrenalism.

Hadassah Medical Organization
P. O. B. 499
Jerusalem, Israel

1908 Montanari, R., & Stockham, M. A. The effect of imipramine on the reserpine toxicity in adrenalectomized rats. *Journal of Pharmacy and Pharmacology*, 1962, 14, 126-127.

Two groups of 12 adrenalectomized male rats received reserpine (5 mg/kg i.p.) 30 minutes after 12 had been given imipramine (25 mg/kg i.p.) to ascertain the effect of imipramine on the mean survival time of 20.4 hours. Imipramine may protect the adrenalectomized rat from reserpine toxicity by inactivating the 5HT which is released.

Laboratory of Chemical Pharmacology
National Heart Institute
NIH
Bethesda, Md.

1909 Maling, H. M., Highman, B., & Pector, S. Neurologic, neuropathologic, and neurochemical effects of prolonged administration of phenylisopropylhydrazine (JB 516), phenylisobutylhydrazine (JB 835) and other monoamine oxidase inhibitors. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 335-343.

The effects of the administration of pheniprazine phenylisobutylhydrazine (JB 835), and other MAO inhibitors on dogs, cats, squirrel monkeys and rabbits were studied. Animals were given daily doses of drugs i.c. or p.o., 5 days a week. In dogs typical pheniprazine doses were 0.4-1.6 mg/kg i.c. or 3.2 mg/kg p.o. Prolonged administration of pheniprazine or JB 835 consistently produced marked neurological effects in dogs, including ataxia, tremors, nystagmus and impaired motor coordination. Most dogs developed neurological lesions, usually in the inferior olivary nucleus, or in the pyriform lobe, or both. The 1 sign most completely associated with a lesion in the inferior olivary nucleus was nystagmus. Pyridoxine did not prevent the neurological signs or lesions. Such lesions were not found in cats, rabbits and squirrel monkeys, or in dogs given inhibitors other than pheniprazine. Cats and squirrel monkeys showed impaired motor coordination but not nystagmus. Dogs showed markedly elevated serotonin and unchanged levarterenol levels in brain stem and spinal cord after the last administration of other potent MAO inhibitors (iproniazid, isocarboxazid, nialamide, iproniazid, parveline and amphetamine). These findings demonstrate the danger of delayed toxicity with the chronic administration of some drugs.

Laboratory of Experimental Pathology
National Institute of Arthritic and Metabolic Diseases
Bethesda, Md.

1910 Douglas, J. F., Ludwig, R. J., & Schlosser, A. The metabolic fate of carisoprodol in the dog. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 1-27.

Longrel dogs, fasted overnight, had an indwelling catheter placed in the femoral vein,

and a propylene glycol-water solution of carisoprodol, 5.1 or 8.0 mg, labeled in the carbonyl position with C^{14} , administered i.v. Urine was collected and 3 ml volumes of blood were withdrawn through the catheter at appropriate intervals. In the dog, carisoprodol is largely metabolized to a compound tentatively identified as hydroxycarisoprodol. Hydroxymeprobamate and small quantities of meprobamate also occur in the urine. Carisoprodol itself is excreted unchanged in trace amounts. After i.v. administration of carisoprodol to dogs, the major circulating carbamate is the unchanged drug. Hydroxycarisoprodol, hydroxymeprobamate and meprobamate are also present in the blood.

Wallace Laboratories
Cranbury, N. J.

1911 Koechlin, Bernard A., Schwartz, Morton A., & Oberhaensli. Metabolism of C^{14} -iproniazid and C^{14} -isocarboxazid in man. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 11-20.

The metabolic fates of iproniazid labeled in the isopropyl group at C_2 and isocarboxazid labeled in the benzyl moiety in human subjects were investigated and compared to previous results in rats. Both drugs were rapidly absorbed after oral administration of therapeutic doses. C^{14} -Isocarboxazid was metabolized by oxidation of the labeled isopropyl substituent resulting in the elimination of 50-60% of the radioactive dose as pulmonary carbon dioxide within 24 hours. The oxidation rates differed markedly between individuals as did the patterns of the radioactive urinary excretion products. C^{14} -Isocarboxazid was metabolized analogously by oxidation of the labeled benzyl moiety to C^{14} -benzoic acid which was excreted as urinary C^{14} -hippurate and accounted for 56% of the dose in 24 hours. Comparison of the fate of the 2 drugs in man with that in rats revealed identical major pathways of oxidative degradation but characteristic differences of the degradation rates. Much higher doses of both drugs are required in the rat than in man to elicit measurable pharmacological effects. In both species isocarboxazid seemed to be oxidized faster than iproniazid.

while faster rates of oxidation of both drugs in the rat than in man were indicated.

Department of Pharmacology
Hoffmann-La Roche Inc.
Nutley, N. J.

1912 Albaum, Harry G. The effect of central nervous system drugs on the enzyme activity of rat brain. *Acta Neurologica Scandinavica*, 1962, 38, 68.

The effect of 5 psychoactive drugs [concentrations unspecified] on 10 CNS enzyme systems were studied in rat brain tissue. Significant alterations of enzyme activity were observed with pentobarbital (malic dehydrogenase and hexokinase), meprobamate (hexokinase and lactic dehydrogenase) and reserpine (enolase and myokinase). None of the drugs affected aldolase, glutamic oxalacetic transaminase, glutamic pyruvic transaminase, phosphoglycerokinase or transaminase, phosphoglycerokinase or glyceraldehyde phosphate dehydrogenase. In view of the fact that both of the rate-limiting steps in glycolysis were unaffected by drugs, it seems highly unlikely that these drugs exert their metabolic effects on the glycolytic sequence.

Department of Biology
Brooklyn College
Brooklyn, New York, N. Y.

1913 Martin, W.R., & Eisenman, A.J. Interactions between nalorphine and morphine in the decerebrate cat. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 113-119.

Acute physical dependence can be produced by a single dose of morphine in the decerebrate cat and the acute abstinence syndrome of the acutely physically dependent cat consists of a sequence of changes in respiratory and cardiovascular functions that are similar to the changes observed in severely narcotized subjects treated with nalorphine. Morphine (11-20 mg/kg) decreased respiratory rate, respiratory minute volume, pulse rate and blood pressure, increased serum CO₂ concentration and decreased serum pH in the decerebrate cat. Nalorphine (5-10 mg/kg) in contrast produced a moderate increase in respiratory rate and minute volume, and a modest decrease in serum CO₂ and blood pressure. Nalorphine when administered to decerebrate cats severely depressed by morphine produced a transient and

marked increase in respiratory rate, minute volume, blood pressure and pulse rate which gradually subsided to an equilibrium state characterized by normal pulse rate and blood pressure and a slight tachypnea. At equilibrium, serum CO₂ is lower than the control level and serum pH is slightly elevated. Nalorphine exerts a direct stimulant action on the respiratory system, antagonizes certain effects of morphine and unmasks acute physical dependence.

NIMH Addiction Research Center
PHS Hospital
Lexington, Ky.

1914 Zimmerman, George B. Megacolon from large doses of chlorpromazine. *Archives of Pathology*, 1962, 74, 47-51.

Sprague-Dawley, Long-Evans and cross-breeds of these two strains of rats were given 46 mg/kg chlorpromazine i.p. The total number of injections and temporal spacing varied, but most animals had 1-3 injections at intervals of about 1 month. Only those surviving the initial injection for more than 4 weeks were considered; 99 rats met this condition. Megacolon was judged by degrees of abdominal distention recorded as 0 to 4 plus. Megacolon developed in 41 out of the 99 rats. Males developed megacolon more frequently and more severely. Earliest onset was detectable 7 days after the initial injection. Megacolon was transient in a few but in others persisted for as long as 3 1/2 months after the last injection. Average time of appearance was 11 days. Also some rats developed priapism and seminal incontinence. No drug-caused histopathology was noted. Bethanechol chloride solution administered to 3 rats with megacolon had no effect on megacolon or bowel function. Megacolon did not develop in guinea pigs given similar large doses of chlorpromazine i.p., nor did it develop in rats given chlorpromazine i.m. or by stomach tube. Reports of "constipation" from patients receiving chlorpromazine may indicate similar effects in humans although therapeutic doses are less than half of those used in the experiment.

Department of Pathology
College of Medicine
University of Iowa
Iowa City, Iowa

915 Highman, Benjamin, & Maling, Harriet M. Neuropathologic lesions in dogs after prolonged administration of phenylisopropylhydrazine (JB 835). *Journal of Pharmacology and Experimental Therapeutics*, 1962, 37, 344-355.

Prolonged administration of pheniprazine (JB 516) and hydrazine (JB 835) produced bilaterally symmetrical neurologic lesions involving the inferior olivary nucleus and, less frequently, the pyriform lobe, particularly the amygdaloid nuclei. Pheniprazine (0.16-1.6 mg/kg s.c. or 3.2 mg/kg p.o.) was administered from 2.5 to 52 weeks. Hydrazine (3.3 mg/kg s.c.) was administered for 4-5 weeks. In the inferior olivary nucleus many neurons had vacuolated cytoplasm. Lesions were present in the pyriform lobe. No such lesions were found in rats, rabbits and squirrel monkeys given these 2 hydrazine inhibitors and no such lesions were found in dogs following other MAO inhibitors. Vestibular degeneration and hemolytic effects were also noted in dogs. These effects are considered to be nonspecific and nonrelated to the brain lesions.

Laboratory of Experimental Pathology
National Institute of Arthritic and Metabolic Diseases
Bethesda, Md.

916 Fink, Gregory B., & Larson, Robert E. Some determinants of amphetamine toxicity in aggregated mice. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 137, 361-364.

Male CF 1 mice received 15-60 mg/kg amphetamine i.p. The mice were given the drug and allocated to a 5- or 10-cage population and to a size A or B cage in a randomized manner. A count on the number of dead mice per cage was made after 4 hours. The ambient temperatures used were 20, 22.5, 25 and 27.5°C. Also some mice were confined in small cannisters (radius 3.2 cm, height 10 cm). The toxicity increased in aggregated mice with greater body weight but remained relatively constant as the dose was increased from 15 to 60 mg/kg. An increase in the number of mice from 5 to 10 per cage (degree of aggregation) greatly increased the toxicity

of amphetamine. Within a temperature range of 20 to 27.5°C each 2.5°C rise in temperature produced a significant increase in amphetamine toxicity. A significant interaction occurred between degree of aggregation and temperature. The size of the cage in which the mice were confined (degree of confinement) had little influence on the toxicity of amphetamine in mice grouped 10 per cage. A decrease in cage size augmented amphetamine toxicity in mouse groups of 5 per cage.

College of Pharmacy
Washington State University
Pullman, Wash.

1917 Clausen, Ebba. Fenacetins og acetylsalicylsyres nefrotoksiske effekt belyst ved dyrekperimentelle undersøgelser. [The nephrotoxic effect of phenacetin and acetylsalicylic acid in animal experiments.] *Nordisk Medicin*, 1962, 67, 755.

Ten rabbits were given phenacetin, 10 acetylsalicylic acid and 8 placebo. After 11 months of daily feeding [dosage unspecified] 1/2 of the animals in each group were injected i.v. with a coliform bacterium. Histopathologically, both the phenacetin and acetylsalicylic acid groups showed dilatation of the tubules, interstitial hyperplasia with round-cell infiltration and abscess formation. Similar histopathologic changes were observed in all animals which had not been given a bacterial suspension. In the placebo-bacteria and in the uninoculated group some inflammation was noted in 1 out of 4 and 2 out of 4 animals, respectively. Kidney damage may be due to direct drug toxicity or to a lowering of resistance to infection.

[No address]

1918 Chusid, Joseph G., & Kopeloff, Lenore M. Chlordiazepoxide as an anticonvulsant in monkeys. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 109, 546-548.

Chlordiazepoxide was tested in 11 rhesus monkeys, 5 of which had been made chronically epileptic by the application of alumina

cream to the cerebral cortex. The drug was injected i. v. (0.55-35 mg/kg) and followed 1/2 hour later by an i. m. injection of pentetrazol (24 mg/kg for epileptic and 64 mg/kg for normal monkeys). Intravenous chlor-diazepoxide in large doses prevented clinical and EEG convulsant effects of the challenge pentetrazol doses in both epileptic and normal monkeys. The only toxicity noted was transient hematuria on 3 occasions in 2 monkeys at the highest dosage (35 mg/kg).

Department of Bacteriology
New York State Psychiatric Institute
New York City, N. Y.

1919 Greef, K., Kasperat, H., & Osswald, W. Paradoxe Wirkungen der elektrischen Vagusreizung am isolierten Magen- und Herzvorhofpräparat des Meerschweinchens sowie deren Beeinflussung durch Ganglienblocker, Sympathicolytica, Reserpin und Cocain. [Paradoxical effects of electrical stimulation of the vagus in isolated guinea pig stomach- and atrium preparations, and the effects of ganglionic blocking agents, sympathicolytics, reserpine and cocaine.] Archiv für Experimentelle Pathologie und Pharmakologie, 1962, 6, 528-545.

Tests were performed on 28 isolated stomachs and over 70 isolated atria from guinea pigs, as well as on a few preparations of guinea pig and rabbit ileum, and cat and rabbit atria. Pretreatment of the isolated guinea pig stomach with atropine and histamine reverses the usual effect of electrical stimulation of the vagus or injection of dimethylphenylpiperazinium iodide, which produces paradoxical inhibition of gastric contraction. This paradoxical effect can be prevented by addition of hexamethonium (10 µg/ml), azamethonium (30 µg/ml), chlorisondamine (5 µg/ml), thymoxyalkylamine (10-20 µg/ml), darethin (10-20 µg/ml) and cocaine (2.5-5 µg/ml), but not by pretreatment of the animals with reserpine (1 mg/kg b. i. d. for 2 days). Similar effects were obtained in the isolated ileum. In the isolated atrium, atropine again reverses the usual inhibitory effects of vagal stimulation, resulting in a positive inotropic and chronotropic action. This paradoxical effect can be prevented by pretreatment with reserpine or by addition of hexametho-

nium, chlorisondamine or nicotine, but is potentiated by dibenzylamine (10 µg/ml), phentolamine (5-10 µg/ml) and cocaine. Some of the interactions of reserpine, butyrylcholine, epinephrine, methamphetamine, tyramine and guanethidine on these preparations are also discussed.

Pharmakologisches Institut der Medizinischen Akademie
Düsseldorf, Germany

1920 Baruk, H., & Launay, J. Action du chlorhydrate de prothipendyl sur le comportement psychomoteur du singe. Comparaison avec l'action de la chlorpromazine. [The action of prothipendyl chlorhydrate on the psychomotor behavior of monkeys. A comparison with the action of chlorpromazine.] Annales Médico-Psychologiques, 1962, 1, 120, 638.

In monkeys, 5 mg/kg prothipendyl caused sedation with diminution in aggressiveness, drowsiness without the induction of deep sleep, and a general slowing of movements. At high doses (20 mg/kg) catalepsy was induced. However the catatonigenic qualities of prothipendyl are less than those of chlorpromazine.

[No address]

1921 Volle, Robert L. Enhancement of postganglionic responses to stimulating agents following repetitive preganglionic stimulation. Journal of Pharmacology and Experimental Therapeutics, 1962, 136, 68-74.

Experiments were conducted on the superior cervical ganglia of urethane-anesthetized cats. Acetylcholine, carbamylcholine, tetramethylammonium chloride (TMA), hexamethonium and procaine were administered, either by rapid injection or by infusion, into the common carotid artery before and after repetitive preganglionic stimulation. Postganglionic responses to acetylcholine, carbamylcholine and TMA were enhanced markedly following repetitive preganglionic volleys at frequencies ranging from 5-100 cps for durations of 10 seconds to 5 minutes. Both amplitudes and time

courses of the responses were increased by the conditioning procedure. Hexamethonium administered in amounts far in excess of those required to produce complete ganglionic blockade had no effect on the development of the enhanced responses. Previous administration of procaine prevented the development of the enhanced responses.

Department of Pharmacology
University of Pennsylvania
Philadelphia, Pa.

1922 Chin, Jane Heng, & Smith, Cedric M. Effects of some central nervous system depressants on the phasic and tonic stretch reflex. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 276-283.

The Achilles tendons of decerebrate cats were sectioned and attached to a force-displacement transducer mounted on the piston of a hydraulic ram. The stretch was produced by displacing the transducer 6 mm distally at a constant velocity of 135 mm/second; the stretch was maintained for 10 seconds and repeated once every 30 seconds (Smith et al., 1962). Mephenesin, caramiphen, pentobarbital, zoxazolamine, carisoprodol, chlorpromazine and scopolamine were given (20-40 mg/ml solutions). Dose-response relationships were established by plotting the percent of the control phasic and tonic reflex vs. log dose. All of the agents produced greater depression of the tonic reflex than of the phasic although some produced an initial enhancement of the reflex. Mephenesin (6.25-100 mg/kg) had relatively greater depressant effects upon the tonic reflex than on the initial phasic component. Low doses of caramiphen (2.5 mg/kg) produced a decrease of both reflexes. Pentobarbital (0.5 mg/kg) and chlorpromazine (0.5 mg/kg) had quite similar effects. The difference in degree of depression of the phasic and tonic reflex components was most marked with mephenesin and least with pentobarbital. The effects of caramiphen resembled those of mephenesin. Carisoprodol, zoxazolamine and chlorpromazine had relative effects upon the 2 components intermediate between the extremes observed with mephenesin and pentobarbital. Only limited depression of the tonic reflex with no

depression of the phasic component was seen after doses of scopolamine which produce cholinergic blockade at peripheral autonomic sites. The order of potency of the agents in producing 50% depression of the tonic reflex was: zoxazolamine, mephenesin, carisoprodol, caramiphen, pentobarbital, chlorpromazine, and scopolamine. Scopolamine was approximately 20 times as potent as zoxazolamine. For 75% depression of the tonic component of the reflex the order of potency was: zoxazolamine, carisoprodol, mephenesin, caramiphen, scopolamine, pentobarbital and chlorpromazine. Chlorpromazine was almost 16 times as potent as zoxazolamine.

Department of Pharmacology
University of Illinois College of Medicine
Chicago, Ill.

1923 Mulé, S. J., & Woods, L. A. Distribution of N-C¹⁴-methyl labeled morphine: I. In central nervous system of nontolerant and tolerant dogs. *Journal of Pharmacology and Experimental Therapeutics*. 1962, 136, 232-241.

N-C¹⁴-methyl labeled morphine was synthesized with a specific activity of about 0.4 mc/mM. Selected areas of the CNS of dogs were separated into gray and white matter where possible; recoveries of 15-150 mμ/g and 150-1500 mμ/g of labeled morphine from dog brain tissues were approximately 90 and 95%, respectively, and recoveries of 50-4000 mμ/g from suitably diluted plasma and urine were ca. 95 and 99%, respectively. Total radioactivity was determined in toluene extracts, employing descending paper chromatography as an additional control procedure. Concentrations of free labeled morphine were lower in the CNS of tolerant dogs in comparison to nontolerant dogs at various intervals of time after a single 2 mg/kg s.c. injection of labeled drug. The levels of free morphine in the CNS of tolerant dogs following consecutive 2 mg/kg s.c. injections as compared to consecutively injected nontolerant dogs were higher at 35 minutes, similar at 4 hours, and much lower at 8 hours. Generally the cerebral cortical gray matter contained the highest concentrations of free morphine in both nontolerant

and tolerant dogs. Predominantly cellular subcortical areas of the CNS occasionally contained levels of free morphine equal to cerebral gray matter values. Cerebral and cerebellar white matter levels of free morphine were lower than gray during the early time intervals and approximately the same as gray matter or higher at later time periods. Small quantities of conjugated morphine were observed in the temporal cortex of nontolerant and tolerant dogs. The rate of disappearance of free morphine from plasma and CSF was faster in tolerant than in nontolerant dogs following a single injection of labeled morphine. Egression of free morphine from plasma and CSF following consecutive labeled morphine injections were quite similar in nontolerant and tolerant dogs. Conjugated morphine levels in plasma were much lower in tolerant dogs as compared to corresponding values in nontolerant dogs after consecutive injections. The differences in the physiological disposition of free morphine between nontolerant and tolerant dogs do not appear to be of sufficient magnitude to account for tolerance development.

Department of Pharmacology
University of Michigan Medical School
Ann Arbor, Mich.

1924 Mulé, S. J., Woods, L. A., & Mellett, L. B. Distribution of N-C¹⁴-methyl labeled morphine: II. Effect of nalorphine in the central nervous system of nontolerant dogs and observations on metabolism. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 242-249.

The effect of nonlabeled nalorphine on the distribution of labeled morphine in the CNS (nalorphine-morphine antagonism), and the chromatographic analysis of the CNS and urinary extracts of nontolerant and tolerant dogs following the administration of labeled morphine was studied. The s.c. administration of labeled morphine (2 mg/kg) before nonlabeled nalorphine (2 mg/kg), given s.c., resulted in a significant increase in the CNS levels of morphine in nontolerant dogs. Simultaneous injection of both drugs, or pretreatment with nalorphine resulted in an increase or no change in morphine levels in nontolerant dogs compared to morphine

control dog values. Effect of nalorphine on the plasma and CSF concentrations of free morphine was somewhat variable. Paper chromatographic studies provided no evidence for the presence of an N-C¹⁴-methyl labeled metabolite of morphine in the CNS or urinary extracts of nontolerant and tolerant dogs.

Department of Pharmacology
University of Michigan Medical School
Ann Arbor, Mich.

1925 Anderson, E. G., Markowitz, S. D., & Bonnycastle, D. D. Brain 5-hydroxytryptamine and anticonvulsant activity. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 179-182.

Electroshock seizures were induced in male Sprague-Dawley rats. An animal was considered protected against the shock on failure to manifest a maximal extensor reflex (MER). Diphenylhydantoin (12.5 mg/kg), pheniprazine (4 mg/kg) and 5HTP (100 mg/kg) were administered i.p. The comparison of relative drug induced effects on the MER in response to electroshock and rise in brain 5HT showed a complete lack of correlation. 5-Hydroxytryptamine elevation alone may play no significant role in the production of the anticonvulsant effect; however, with a better knowledge of the factors relating to binding and release and precise localization in the CNS it is possible that such relationships can be reassessed.

Department of Pharmacology
Seton Hall College of Medicine and Dentistry
Jersey City, N. J.

1926 Green, Harry, Greenberg, Samuel M., Erickson, Robert W., Sawyer, John L., & Ellison, Theodore. Effect of dietary phenylalanine and tryptophan upon rat brain amine levels. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 174-178.

Female weanling Long-Evans rats were used in the study of dietary effects of phenylalanine and tryptophan on brain amine levels. The basal diet was modified with respect to these amino acids. Diets enriched

with phenylalanine contained 9 times the conventional content, while diets enriched with tryptophan contained 5 times the amount present in the basal diet. However, the dl forms of the acids were used. Additionally, the MAO inhibitor tranylcypromine (2.5 mg/kg) was administered orally b.i.d. to half the animals starting with the 8th day of the 5-17 day dietary regimen. Brain levarterenol concentration was not significantly influenced by changes in the phenylalanine and/or tryptophan contents of the diet. Brain dopamine concentration, however, was markedly increased in rats maintained on diets enriched with phenylalanine, but not significantly affected by a deficiency of dietary phenylalanine or by variations in tryptophan dietary content. The 5HT brain level appeared to vary directly with the relative content of dietary tryptophan and inversely with the relative content of dietary phenylalanine. The ability of tranylcypromine to increase the concentration of brain amines was significantly influenced by the dietary content of the 2 amino acids. In general, significantly greater increases of brain 5HT concentration were achieved on diets enriched with tryptophan. Also markedly higher concentration of brain dopamine resulted from diets enriched with phenylalanine. However diets enriched with phenylalanine yielded increases in brain levarterenol concentration which were not substantially different from increases caused by only tranylcypromine. No significant differences in spontaneous motor activity patterns were observed on any schedule.

Research and Development Division
Smith Kline & French Laboratories
Philadelphia, Pa.

1927 Trendelenburg, U., & Weiner, N.
Sensitivity of the nictitating membrane after various procedures and agents. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 152-161.

The sensitivity of the nictitating membrane of the spinal cat to levarterenol, tyramine and acetylcholine was determined after denervation (ablation of the right superior cervical ganglion), decentralization, reserpine, chlorisondamine, TM 10 (choline 2,6-xylyl ether bromide) and phenoxyben-

zamine, pretreatments known to affect the sensitivity and/or levarterenol content of this organ. No relationship was found between the sensitivity to levarterenol and the levarterenol content. Hypersensitivity to levarterenol appeared whenever, for a period of 7-14 days, the nictitating membrane was deprived of the usual influence of tonic impulses. This was observed after chronic denervation, chronic decentralization, or 7 days of pretreatment with reserpine, TM 10 or chlorisondamine. Brief depletion, caused by pretreatment with a single large dose of reserpine, did not cause hypersensitivity. Hypersensitivity to i.a. injections of acetylcholine paralleled that to levarterenol in these procedures. Hyposensitivity to tyramine was observed after any type of depletion of levarterenol stores, whereas hypersensitivity to this substance was found when the levarterenol stores were normal or only slightly affected. Thus tyramine acts by liberating endogenous levarterenol. Prolonged reserpine pretreatment does not increase the plasma half-life of injected levarterenol.

Department of Pharmacology
Harvard Medical School
Cambridge, Mass.

1928 Smith, Cedric M., Budris, A. V., & Paul, J. W. Quantification of phasic and tonic stretch reflexes: effects of neuromuscular blocking agents. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 267-275.

In order to determine if any curariform agent produces selective blockade of the mammalian intrafusal neuromuscular junction, experiments were performed on pentobarbital anesthetized cats suspended in a stereotaxic apparatus. Transection of the brain stem at the level of the colliculi was accomplished by electrocoagulation, the cauterized area corresponded to that area encompassed by the following stereotaxic coordinates: anterior 1 to posterior 1, right lateral 6 to left lateral 6 and vertical -8 to +4. Of 80 animals operated upon 45 died within the 1st 24 hours and 40 of these died within the 1st 12 hours (hemorrhage at the site of the lesion). Rigidity appeared in the survivors 6-8 hours after section with

recovery from the pentobarbital anesthesia. Results were obtained with 25 out of 35 cats which exhibited extensor tone. Reflex contractions of the gastrocnemius and soleus muscles to stretch were obtained and contractions of the contralateral muscles induced by tetanic sciatic nerve stimulation were recorded. The total tension developed upon stretching was characterized by initial peak contraction (phasic) with a decrement to a lower sustained tension (tonic). Muscle tension obtained after section of the sciatic nerve or after succinylcholine-induced neuromuscular blockade was taken as a measure. Cumulative dose-effect relationships for depression of the above responses were established for tubocurarine, decamethonium and 4 polymethylene bis-isoquinolinium derivatives. Tubocurarine produced depression of the sustained tetanic nerve-muscle response followed, in order of inhibition, by the initial tetanic response, the tonic reflex, the twitch, and finally, the phasic reflex. The sustained tetanic response was 8 to 9 times more sensitive than the phasic reflex or twitch response. The patterns of effects of the 4 bis-isoquinolinium derivatives were similar to those of tubocurarine. In contrast, given doses of decamethonium produced almost equal inhibition of all the responses assessed. The postulate that these agents act primarily at the neuromuscular junctions of extrafusal muscle fibers and that any depression of the fusimotor nerve-muscle transmission takes place with doses equal to or larger than those required to block extrafusal junctions appears true.

Department of Pharmacology
University of Illinois College of Medicine
Chicago, Ill.

1929 Chai, C.K., Roberts, Eugene, & Sidman, Richard L. Influence of aminooxyacetic acid, a γ -aminobutyrate transaminase inhibitor, on hereditary spastic defect in the mouse. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 109, 491-495.

Homozygous spastic mice (spa/spa) were tested for righting time, tremor, flexibility of trunk movement and alertness. Diphenylhydantoin (50 μ g per mouse),

trimethadione (a 100 μ g dose) and aminooxyacetic acid (AOAA; 5-30 μ g), were given i.p. Paper chromatography was conducted on brain extracts. When single doses of these drugs were administered only AOAA was effective in decreasing symptoms. Subcutaneously injected AOAA (5-15 μ g/g) produced a marked improvement which was the same for 12-24 hours or more. In some animals which received continued injections of the drug there was a depression of motor activity, decreased alertness and loss of weight. Brain extracts showed no significant alteration in the distribution of ninhydrin-positive constituents in comparison to normal.

Roscoe B. Jackson Memorial Laboratory
Bar Harbor, Me.

1930 Green, Harry, Sawyer, John L., Erickson, Robert W., & Cook, Leonard. Effect of repeated oral administration of monoamine oxidase inhibitor on rat brain amines. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 109, 347-349.

Repeated daily oral administration of tranlylcypromine (5 mg/kg b.i.d.) or iproniazid (50 and 100 mg/kg b.i.d.) to rats for 3-10 days resulted in cumulative increases in brain 5 HT concentration 2-4 times that produced by a single administration of the drug. Levarterenol concentration was not appreciably different from that following a single drug administration. The rats showed no overt pharmacologic responses. No significant or consistent effect upon the motor activity pattern of drug-treated rats compared to untreated rats was observed.

Research and Development Division
Smith Kline and French Labs.
Philadelphia, Pa.

1931 MacKenzie, Robert D., & McGrath, W. Robert. Absorption of thalidomide in the rat. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 109, 511-515.

Radioactive thalidomide (C^{14} in one of the carbonyl groups of the phthaloyl moiety; 4.7 μ c/mg) was administered orally at a dose of 10 mg/kg to groups of rats. These were sacrificed at selected intervals, and blood and brains collected for analysis. Thalidomide is rapidly absorbed from the gastrointestinal tract. The peak blood level appeared in 15 minutes and the peak brain level in 30 minutes to 1 hour. Excretion data indicate that at least 40% of the labeled material is absorbed over a dosage range of 10-100 mg/kg. Urinary and fecal excretion of the label occurred rapidly and the amount remaining in the animals 48 hours after administration averaged 10% of the dose or less.

Scientific Laboratories
Wm. S. Merrell Co.
Division of Richardson-Merrell Inc.
Cincinnati, Ohio

1932 Swinyard, Ewart A., Radhakrishnan, N., & Goodman, Louis S. Effect of brief restraint on the convulsive threshold of mice. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 337-342.

The effects of brief periods of body restraint on alternating current electroshock, low frequency electroshock and i.v. pentetrazol seizure thresholds was investigated in male CF₁ mice. Restraint significantly lowered thresholds as measured by all 3 techniques; maximal effect was observed almost immediately after restraint. Adaptation to the effect of restraint occurred rapidly. In adrenalectomized mice restraint had no such lowering effect on the seizure threshold. A small dose of i.v. epinephrine (0.125 μ g/g) lowered all 3 thresholds to a similar extent. Also brief periods of restraint rapidly induced hyperglycemia. The observed increase in brain excitability caused by restraint is the result of endogenously released epinephrine on the CNS.

Department of Pharmacology
University of Utah
College of Pharmacy and Medicine
Salt Lake City, Utah

1933 Eerola, Risto. The combined action of morphine and atropine. *Annales Medicinæ Experimentalis et Biologiae Fenniae*, 1962, 40, 83-90.

Male mice were injected s.c. with varying amounts of morphine and/or atropine. Twenty-four hour toxicity was studied, i.e., lethality between 5 and 95% (LD₅ and LD₉₅). For atropine, mortality fluctuated between 10 and 85% and the LD₅₀ was established at 400 mg/kg. For morphine, mortality fluctuated between 10 and 90% and the LD₅₀ was 300 mg/kg. For the combination of drugs mortality ranged from 15 to 100%. Here the doses were presented in a rectangular coordinated system according to Gaddum (1959). The lethality areas of the individual drugs were presented by thickened segments of the coordinative axis. This analysis revealed an additive synergism between morphine and atropine.

Institute of Pharmacology
University of Helsinki
Helsinki, Finland

1934 Casier, H., & Merlevede, E. On the mechanism of the disulfiramethanol intoxication symptoms. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 165-177.

Arterial blood pressure, heart rate and respiration were followed in morphinized, chloralosed dogs. Disulfiram (0.05%) was infused into the femoral vein at a rate of 4 ml/minute; no reactions were observed after 25 mg/kg. In other experiments ethanol (133-960 mg/kg) and acetaldehyde (3.3-5.0 mg/kg) were infused with and without disulfiram. Administration of a compound obtained by the chemical reaction in vitro between disulfiram and ethanol induces all the physical symptoms provoked by the administration of disulfiram and ethanol. Disulfiram, i.v., induced a marked and prolonged output of carbon disulfide in the expired air. Neither acetaldehyde nor the metabolites of disulfiram, diethyldithiocarbamate, diethylamine and carbon disulfide, are responsible for the acute toxic effects encountered. The positive compound obtained in vitro is probably a quaternary

ammonium base.

J.F. Heymans Institute of Pharmacology
University of Ghent
Ghent, Belgium

1935 Drucker, William R., Kingsbury, Bryant, Powers, Adie, & O'Reilley, Mark. Metabolic changes in lethal shock produced by norepinephrine. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 871.

Variable amounts of l-levarterenol (norepinephrine; 1.9-4.8 μ g/kg/minute) were given as a 4-hour constant i. v. infusion to 10 well fed normovolemic dogs. Serial analyses were made of blood glucose and carbohydrate intermediaries, arterial pH, blood volume, hematocrit, and arterial pressure. All animals manifested a similar rise in blood pressure, blood glucose (20 to 90 mg%), pyruvic acid (1 to 2 mg%), and inorganic phosphate (407 mg%). The 5 dogs in which the infusion of levarterenol exceeded 2.6 μ g/kg/minute died. Death occurred from 1/2 to 30 hours following discontinuation of the infusion and was associated with a gradual decline in blood pressure and pH with an accumulation of lactic acid (over 100 mg%). These changes began during the infusion. By contrast, there was neither a rise in excess lactate nor a fall of pH in the survivors. Blood volume fell in 8 of 10 dogs during the infusion and remained low for several hours thereafter; the mean fall was 11% for nonsurvivors and 16% for survivors. Similar metabolic changes are characteristic of the severe oligemic and hypotensive phase of hemorrhagic shock. Here these changes were produced by the severe vasoconstriction caused by levarterenol with minimal hypovolemia and similar fatal consequences.

[No address]

1936 Winter, D., & Timar, Magda. Experimentelle Untersuchungen über das Wiedereinschlafen aus der Barbituratnarkose erwachter Tiere. [Experimental studies on the rehypnosis of animals just

awakened from barbiturate anesthesia.] *Pharmazie*, 1962, 17, 454-455.

The number of rats falling back to sleep when a 2nd drug was given i. v. immediately upon awakening from the anesthesia produced by 100 mg/kg of sodium amobarbital i. p. (lasting 71 ± 5 minutes) varied from 80-100% for chlorpromazine (2 mg/kg), imipramine (10 mg/kg), serotonin (1.25 mg/kg), epinephrine (0.05 mg/kg) and acetylcholine (0.1 mg/kg) to 40-60% for imipramine (5 mg/kg), methocarbamol (125 mg/kg), reserpine (5 mg/kg), methylcellulose (125 mg/kg), heparin (250 U), histamine (0.01 mg/kg) and diethylaminoethylbenzylate (5 mg/kg) and to 0% for reserpine (1 mg/kg), dimethylaminoethyl-p-acetamidobenzoate (5 mg/kg), procaine (12.5 mg/kg) and polyvinylpyrrolidone (175 mg/kg). A 2nd dose of amobarbital produced rehypnosis in 20% at 7 mg/kg and 100% at 15 mg/kg. This technique is not adequate as a specific test to distinguish narcosis-potentiating agents from neurotropic drugs with additive effects.

Pharmaceutical Division
Chemical-Pharmaceutical Research
Institute
Bucharest, Romania

1937 Buchel, L., Levy, Jeanne, & Tanguy, O. Rapport entre constitution chimique et action pharmacologique. Influence de la nature de l'amine sur les propriétés pharmacologiques dan quelques amino-esters $X-CO_2(CH_2)_2-N<$ et quelques amino-esters phenoliques $Y-O(CH_2)_2-N<$. [Relationship between chemical constitution and pharmacological activity. Effect of the nature of the amine on the pharmacological properties in some amino-esters $X-CO_2(CH_2)_2-N<$ and some phenolic amino-ethers $Y-O(CH_2)_2-N<$.] *Archives des Sciences Physiologiques*, 1962, 16, 57-70.

A comparison of the diethylamino-, piperidyl- and methyl-4-piperazinyl-derivatives of either cyclohexyl-1-cyclohexane carboxylic acid ethyl ester or cymene-ethyl ether with respect to their acute toxicity (LD₅₀ i. p.), hypothermic activity and effect on exploratory behavior, chloral hydrate and hexobarbital anesthesia, cylin-

der-climbing behavior, electroshock convulsions and tremorine spasms in mice, and their anticonvulsant and antiatropine effects in rats, showed that the effect of the type of amine substituent differed in the 2 series tested and varied with the pharmacological activity being studied. The amino group had the greatest effect on the spasmolytic properties of the amino esters, the general order of activity being piperidyl- >

diethylamino- > methyl-4-piperazinyl-, while the order was generally piperazinyl- > diethylamino- for the other properties of the amino esters and consistently the opposite for the amino ethers.

Laboratoire de Pharmacologie Chimique
Faculté de Médecine
Paris, France

See also 1716, 1822, 1885, 1897, 1946,
1981

1938 Kaye, Sidney. Simple, reliable tests for some common poisons and drug overdosage. *Clinical Medicine*, 1962, 69, 1971-1975.

Germane to the need for simple reliable tests to detect various poisons and drugs, clinical procedures are delineated for determining the presence of barbiturates, CO, methanol, arsenic, mercury, antimony or bismuth, salicylates, sulfanilamide derivatives and phenothiazine compounds in the human body.

State Health Department
Commonwealth of Virginia
Richmond, Va.

1939 Long, R.F. Reversible inhibition of brain monoamine oxidase in vitro and in vivo. *Acta Neurologica Scandinavica*, 1962, 38, 27-28.

In vitro studies on the action of reversible inhibitors on human brain MAO required different substrates for each inhibitor concentration to reduce the rate of oxidation. With harmaline, 50% inhibition was produced by 10^{-3} M with tryptamine and 2×10^{-7} M with levarterenol or 5HT as the substrate, all substrates stabilized at a concentration of 2×10^{-3} M. Differences were observed, however, among enzyme preparations from the brains of different species both in the relative rates of oxidation of different amines and in their relative affinities as measured by the action of reversible inhibitors. Harmaline or α -methyltryptamine administered to mice in doses which caused marked rises in brain 5HT and levarterenol levels failed to raise the level of dopamine. Since irreversible MAO inhibition produces a rise in dopamine, 5HT and levarterenol levels, it appears probable that the differential increase observed was due to the selective inhibition of MAO by the reversible inhibitors utilized.

Research Department
Roche Products Ltd.
Welwyn Garden City, Great Britain

1940 Baxter, Claude F. Metabolism of γ -aminobutyric acid in vivo. *Acta Neurologica Scandinavica*, 1962, 38, 20.

A constant ratio is found in different areas of guinea pig brain between the level of endogenous GABA and the maximal potential activity of glutamic acid decarboxylase. An exception to this correlation is found in the olfactory lobes which contain a much higher GABA level per unit of decarboxylase activity. Large doses of GABA injected parenterally into rats elevate GABA levels in the olfactory lobes but not in other brain areas. The activity of GABA α -KG transaminase in normal animals appears unrelated to GABA levels found in different areas of the brain. The effect of pyridoxal phosphate antimetabolites and carbonyl trapping agents on α -KG transaminase, GABA transaminase and GABA in brain, and β -alanine in liver has been studied. Within the brain of the intact rat, amino-oxyacetic acid appears to inhibit GABA transaminase without affecting α -KG decarboxylase, while thiosemicarbazide inhibits this decarboxylase preferentially. Both enzymes are equally susceptible to inhibition by either of these compounds in vitro. Differences may be attributable to structural barriers in vivo.

Department of Biochemistry
Medical Research Institute
City of Hope Medical Center
Duarte, Calif.

1941 Van der Helm, H.J. Electrophoretic separation of enzymes in the central nervous system. *Acta Neurologica Scandinavica*, 1962, 38, 64-65. [Summary]

Lactic dehydrogenase isoenzymes from homogenates of human brain were compared with lactic dehydrogenase isoenzymes in CSF and serum. The diagnostic value of enzyme activity in the CSF will be enhanced by such chemical procedures since medicine is currently limited by a rather nebulous understanding of the role played by the CNS in these activities. This approach may also be advantageous in interpreting alterations in CSF enzyme activity. Agar electrophoresis of enzymes is discussed, along

with the possibility of performing these electrophoretic separations on an ultra-micro scale.

Provincial Ziekenhuis
Santpoort, The Netherlands

1942 Klöcking, H.-P., & Walter, H. Ein papierchromatographischer Nachweis von Barbitursäurederivaten auf der Grundlage der modifizierten Murexidreaktion. [A paper-chromatographic technique for determining barbiturates on the basis of the modified murexide reaction.] *Pharmazie*, 1962, 17, 525-526.

Chromatographic studies with phenobarbital, barbital, ethylcrotylbarbituric acid, cyclo-barbital, methylphenobarbital, propallylonal, alloparylbarbital and allobarbital in the system dimethylformamide/benzene-dioxane showed that all but methylphenobarbital could be readily detected in amounts of 20-40 µg by means of a modified murexide reaction following extraction of the paper with absolute ethanol. Nonbarbiturate sedatives such as phenazone, phenacetin, meprobamate, etc. did not give the characteristic color.

Pharmakologisches Institut
Universität Rostock
Rostock, Germany

1943 Večerková, J., Kohlíček, J., & Kácl, K. Die Anwendung papier-chromatographischer Methoden zum toxikologischen Nachweis von Arzneimitteln II. 2. Mitteilung: Über das chromatographische Verhalten des Amidopyrins bei der Analyse von Analgetica-gemischen. [The use of paper chromatographic techniques for the toxicological detection of drugs. II. The chromatographic behavior of amidopyrine during the analysis of mixtures of analgesics.] *Pharmazie*, 1962, 17, 394-399.

The chromatographic behavior of aminopyrine (amidopyrine), phenacetin, phenazone and caffeine was investigated in a mixture of isoamyl alcohol, n-propanol, water and citric acid (50:100:150:3 g) on buffered paper (pH 3.15-4.10) or in cyclohexane and chloroform (10:0-0:10), petroleum and

chloroform (10:0-0:10), petroleum, cyclohexane, CCl_4 , benzene or chloroform on formamide-treated paper. R_f values are given and the separation of these 4 drugs is discussed. The best separation of all 4 components could be achieved with formamide/benzene. All 4 drugs could be detected on the paper with short wavelength UV light, while for aminopyrine and phenazone, Dragendorff's reagent and $\text{K}_3\text{Fe}(\text{CN})_6\text{-FeCl}_3$ were also useful.

Laboratory for Toxicology and
Legal Chemistry
Charles University
Prague, Czechoslovakia

1944 Dreyfus, Pierre M. Microchemical enzyme studies of the rat nervous system in experimental thiamine deficiency. *Acta Neurologica Scandinavica*, 1962, 38, 69-70.

The distribution of thiamine-dependent CNS enzymes was determined in normal and thiamine-deficient rats in various stages of thiamine deprivation to elucidate the selective vulnerability of specific CNS areas to thiamine deficiency. Quantitative histochemical methods facilitated the use of microgram quantities of tissue as well as histological controls. Transketolase activity was estimated by measuring sedoheptulose-7-phosphate production during the incubation of fresh frozen tissue slices or homogenates in a buffered medium containing ribose-5-phosphate as substrate. Sedoheptulose-7-phosphate and ribose-5-phosphate were determined by microspectrophotometric methods. Histological controls, dry weight, fat free dry weight or protein determinations were obtained on all samples. The 1st hour of incubation represented the activity of transketolase, the rate-limiting enzyme, which was manifested by linear Lineweaver-Burke plots. Transketolase activity (μM sedoheptulose-7-phosphate/g protein/minute) was 2.3 in white matter and 1.5 in frontal cortex and sciatic nerve. Enzyme activity in normal rats paralleled total lipid content of the samples. Transketolase activity was considerably diminished in excessive thiamine depletion. Results indicate that the monophosphate shunt may play an important role in developing and maintaining

the functional integrity of the medullated portions of the CNS.

McLean Hospital Research Laboratory
Waverly, Mass.

1945 Cremer, J.E. A study of amino acid metabolism in rat brain using $[C^{14}]$ -glucose and inhibitors. *Acta Neurologica Scandinavica*, Supplement I, 1962, 38, 22-23.

An in vitro comparison of triethyl tin and triethyl lead with other known metabolic inhibitors of the oxidation of C^{14} -labeled substrates by slices of rat brain cortex revealed that the 2 compounds selectively inhibited glucose oxidation. Preliminary in vitro experiments with these 2 compounds and other known inhibitors on the levels of amino acid in brain tissue and their degree of labeling from C^{14} -labeled glucose have shown that for a given inhibitor there is a definite change in the amino acid pattern of brain slices incubated with labeled glucose. Thus, changes in GABA were not necessarily a reflection of changes in glutamic acid. Unlike glutamic acid, the concentration of GABA within a brain slice was not readily lowered in the presence of inhibitors but its specific activity was markedly reduced. Incorporation of C^{14} -labeled amino acids into the protein fraction of brain slices was particularly sensitive to the inhibitors tested.

Toxicology Research Unit
Woodmansterne Road
Carshalton, Surrey
Great Britain

1946 van Rees, H., & Noach, E.L. Reserpine-induced changes in insulin action in the rat. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 264-265.

In intact rats, insulin hypoglycemia was unchanged by concomitant reserpine treatment, and decreased by reserpine pretreatment. In the latter experiment, reserpine was shown to have a long-lasting blood sugar elevating action of its own. The reserpine-induced impairment of insulin activity was proven not due to acute catecholamine release, as it was also present in adrenomedullectomized animals

and after dihydroergotamine pretreatment in such animals. An acute insulin-induced increase in corticosteroid levels could not be excluded by experiments in animals adrenalectomized 14 hours after reserpine pretreatment and 2 hours before insulin administration. Also the enhancing influence of in vitro insulin addition to glucose uptake by isolated rat hemidiaphragms was unmodified by in vivo reserpine pretreatment.

Department of Pharmacology
University of Leyden
Leyden, The Netherlands

1947 Eggels, P.H., Hoekstra, M.H., & Rolkens, P.W.A. The chemical assay of norepinephrine and serotonin in the rat's brain. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 300-302.

Spectrofluorophotometric estimation of levarterenol (norepinephrine) and serotonin in the whole brain of the rat yielded the following concentrations: levarterenol content, ca. 0.50 μ g/g (tissue wet weight) and serotonin content, ca. 0.56 μ g/g. Recovery rates with levarterenol and serotonin added to the tissue ranged from 90-100%. Shore and Olin's (1958) acid purification method gave the same results for serotonin as did the alkaline purification method (Bogdanski), indicating a dearth of 5HT in rat brain. Results obtained with iproniazid and reserpine agreed with those found in the literature.

Department of Pharmacology
University of Utrecht
Utrecht, The Netherlands

1948 Gibbons, James L., & McHugh, Paul R. Plasma cortisol in depressive illness. *Journal of Psychiatric Research*, 1962, 1, 162-171.

Plasma cortisone (cortisol) was measured at weekly intervals in 17 depressed patients. All except 1 case received small amounts of hypnotics (200-400 mg amylobarbitol) because of insomnia. Later treatment consisted of ECT in 12 cases and imipramine in 5, 2 of whom had ECT as well. The

dosage of imipramine was 25-50 mg t.i.d. Two left the hospital prematurely while still obviously depressed and the remaining 16 were considered recovered or greatly improved at the time of discharge. Elevated cortisone levels were found before treatment and generally the more severe the depression the higher the cortisone level. In 13 cases the process of recovery was accompanied by a decline in cortisone levels. One cyclothymic patient was included in the caseload and provided the best evidence for a direct relationship between mood and cortisone level. Here phases of depression were accompanied by high hormone levels, which approached normal when she became well and were quite low in phases of elation.

Department of Psychiatry
Maudsley Hospital
London, S.E. 5, Great Britain

1949 Axelrod, Julius. The enzymatic N-methylation of serotonin and other amines. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 28-33.

An enzyme that transfers the methyl group of S-adenosylmethionine to the amino group of 5HT is described. The enzymatic N-methylation of 5HT was determined by measuring the amount of 5HT-N-methyl- C^{14} formed after incubating the enzyme with 5HT and S-adenosylmethionine- $C^{14}H_3$. Measurements were made with a scintillometer. The enzyme has been partially purified and its properties studied. The 5HT methylating enzyme can N-methylate a variety of normally occurring compounds such as dopamine, normetanephrine, metanephrine, epinephrine, tyramine and octopamine as well as a variety of foreign compounds such as ephedrine, amphetamine, aniline, normorphine, normeperidine and nornicotine. The enzyme is highly localized in the rabbit lung.

Laboratory of Clinical Science
NIMH
Bethesda, Md.

1950 Brown, Donald D., Silva, Omega L., & McDonald. A comparison of the urinary metabolites of l-histidine- C^{14} in schizo-

phrenic and normal subjects. *Journal of Psychiatric Research*, 1962, 1, 101-105.

Twelve schizophrenics and 11 volunteer control subjects were given identical diets for the experiment. Radioactive l-histidine- C^{14} was administered orally to these subjects and the radioactive urinary metabolites were separated by column chromatography and measured by isotope dilution techniques. There was no significant difference between the normal and schizophrenic groups in the fraction of radioactivity excreted, the amount of C^{14} lost after urine concentration, the urinary hydantoin-propionic acid- C^{14} , histidine- C^{14} , l-methylhistidine- C^{14} , or the combined value for free and conjugated radioactive imidazoleacetic acid. No evidence was found for the purpose of qualitative differences in metabolites in the schizophrenic group, nor did any subject in either group lack any of the known major histamine derivatives.

Laboratory of Clinical Science
NIH
Bethesda, Md.

1951 Mueller, Peter S. Plasma free fatty acid concentrations (FFA) in chronic schizophrenia before and after insulin stimulation. *Journal of Psychiatric Research*, 1962, 1, 106-115.

Two series of studies were undertaken involving 12 male chronic schizophrenics without somatic illness and 20 normal male subjects. The same 12 schizophrenics participated in both studies compared to 7 normal volunteers in the 1st and 13 in the 2nd, dealing respectively with plasma FFA and blood glucose before and after 10/U insulin i.m. Both studies were performed after an overnight fast. In both studies preinsulin FFA means of the normal and schizophrenic patients were identical. Mean fasting blood glucose concentrations were significantly higher in the schizophrenic group in the 2nd experiment. No other significant difference was noted in blood glucose. Both groups of subjects had decreases in blood glucose of similar proportions. In both studies all normal subjects had falls in FFA within a very narrow

range. Three patients in the 1st study and 4 in the 2nd had rises or no decreases in FFA after insulin. Eight schizophrenics in the 1st study and 5 in the 2nd had post-insulin FFA concentrations above the highest normal postinsulin FFA. Correlations showed a fair degree of consistency in both studies.

Laboratory of Clinical Science
NIMH
Bethesda, Md.

1952 McDonald, R.K., & Weise, V.K. The excretion of 3-methoxy-4-hydroxymandelic acid in normal and in chronic schizophrenic male subjects. *Journal of Psychiatric Research*, 1962, 1, 173-183.

Urinary vanilmandelic acid (VMA) was assayed by a modification of the tracer technique described by Weise (1961); urinary creatinine was determined by the alkaline picrate method. Seventeen healthy volunteers, 10 chronic and 3 acute schizophrenics, all male, were studied. Significant diurnal changes in VMA excretion rate occurred in both normal and chronic schizophrenic subjects. The VMA excretion rate was greater during the waking hours (8 a.m.-12 p.m.) than during the sleeping hours (12 p.m.-8 a.m.); this difference was not a function of the physical activity attending ordinary ambulatory activity. The chronic schizophrenic subjects tended to have a higher VMA excretion rate than the normal subjects, and the difference in excretion rates was significant when the subjects were kept on a 24-hour period of bed rest. The chronic schizophrenics excreted less creatinine than the normal subjects. This difference may be due to a difference in body composition between the 2 groups. Reserpine administration (2.5 mg i.m.) caused a similar increase in VMA excretion in both groups. Chlorpromazine administration (200 mg p.o.) caused a similar decrease in VMA excretion in both groups.

Laboratory of Clinical Science
NIMH
Bethesda, Md.

1953 Novák, I., Buzás, G., Tóth, L., & Simon, L. Beiträge zur vergleichenden Untersuchung des ungarischen und indischen Hanfes. [A comparative investigation of Hungarian and Indian hemp.] *Pharmazie*, 1962, 17, 95-98; 166-173.

In a 2-part article based on a contribution to a Hungarian symposium on medicinal plants, the authors first discuss the morphology and histology of hemp and then report the results of comparative studies of the ash, sand and moisture content and of the color reactions of approximately 20 varieties of Hungarian and Indian hemp using the alkaline Beam, acid Beam, Ghamrawy, Duquenois-Negm, modified British Pharmacopoea Codex, Rathenasinkam and Viehoveer reactions. The results show that Hungarian hemp contains only traces of physiologically active alkaloids.

Institute of Pharmacognosy
Medical University
Szeged, Hungary

1954 Lewis, J.J., & Van Petten, Garry R. The effect of amphetamine and related compounds on the concentration of adenine nucleotides, inorganic phosphate and creatine phosphate in the rat brain. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 372-377.

Male Wistar rats were given i.p. injections of methamphetamine, amphetamine, dexamphetamine, phenmetrazine (the bitartrate), phenmetrazine, 1-phenmetrazine bitartrate and d-phenmetrazine bitartrate. After 1/2, 1 1/2, 3 or 4 hours, the rats were decapitated and the brain assayed for adenine nucleotides, inorganic phosphate and creatine phosphate, using a spectrophotometer. The order of treatment in each group was randomized, e.g., three 3 x 3 Latin squares. Four hours after treatment with methamphetamine, amphetamine, dexamphetamine, ephedrine, phenmetrazine and d-phenmetrazine there was an increase in the ATP/ADP ratio as a result of the increase of ATP level with concomitant decrease in ADP. The dose required to produce this effect appears to be correlated with the potency

of the drugs as CNS stimulants. Thus 0.45 and 0.90 mg/kg dexamphetamine and methamphetamine caused a ca. 1.5-fold increase in the ATP/ADP ratio, but 10 mg/kg and 20 mg/kg respectively of amphetamine and ephedrine were required to produce an approximately 2-fold increase. Four times the dose of phenmetrazine (1.80 mg/kg) was required to produce an equivalent dexamphetamine (0.45 mg/kg) effect. D-phendimetrazine was about 1/2 as potent as phenmetrazine in its ability to increase brain ATP. The levoisomer of phendimetrazine at the same dosage produced no change. The increase in the ATP/ADP ratio indicates a net increase in ATP resynthesis and that the increased energy thus made available may be a factor in the central stimulant action of these drugs.

Experimental Pharmacology Division
Institute of Physiology
University of Glasgow
Glasgow, Great Britain

1955 Douglas, J.F., Ludwig, B.J., Ginsberg, T., & Berger, F.M. The metabolic fate of mebutamate (Capla). *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 5-9.

Mebutamate (100 mg/kg) was administered p.o. to male dogs and urine samples collected 24-36 hours later. These were extracted with several solvents and assayed through paper chromatography, employing the method of Hoffman and Ludwig (1959) for meprobamate. Three urinary end-products were identified: unchanged drug present in small quantities, a hydroxylated derivative, 2-methyl-2-(β -hydroxyl- α -methylpropyl)-1,3-propanediol dicarbamate, which is the primary metabolite, and a glucuronide conjugate. The toxicity of hydroxymebutamate, the major metabolic product, was evaluated in mice and the LD₅₀ established at 1400 mg/kg in comparison with 460 mg/kg for mebutamate. Hydroxymebutamate appeared to have no other pharmacological properties. The drug concentration in adult human plasma following a 300 mg dose reaches a peak concentration of about 7 μ g/ml in 1-2 hours; the drug half-life in the bloodstream

is ca. 5 hours.

Wallace Laboratories
Cranbury, N.J.

1956 Irwin, Richard L., & Hein, Manfred M. The inhibition of rat brain cholinesterase after administration of the dimethyl-carbamates of deoxy-demethyl-lycoramine, neostigmine or physostigmine. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 136, 20-25.

Male Osborne-Mendel rats were injected i.p. with varying doses (0.084-1.14 mg/kg) of the dimethyl-carbamate of deoxy-demethyl-lycoramine methiodide (MCDL), its tertiary analogue HCDL, neostigmine bromide and physostigmine salicylate. Each surviving animal was decapitated and the entire brain removed (caudal part discarded) and used in the analysis of cholinesterase activity. After the administration of ca. 20 doses (0.108 mg/kg) of MCDL the activity of brain cholinesterase is essentially unchanged. When 1.39 mg/kg of MCDL, the approximate LD 20 of HCDL, was given to 9 rats pretreated with 2.0 mg/kg atropine, none survived. Two of the 5 animals given 0.5 mg/kg atropine and 1.01 mg/kg MCDL survived and had brain cholinesterase values within the normal range. In contrast to MCDL the passage of neostigmine into the brain was detected in 1/3 of the animals, occurring at both 0.069 mg/kg and 0.835 mg/kg. The convulsions and deaths observed after neostigmine or MCDL occurred in 8-15 minutes. Using the tertiary drugs physostigmine or HCDL these effects were observed in 6-9 minutes. After physostigmine a rapid and marked inhibition of brain cholinesterase occurred. Physostigmine was the only drug of the 4 tested which reduced the level of cholinesterase activity in the brain to less than 20%.

National Institute of Neurological Diseases
and Blindness
NIH
Bethesda, Md.

1957 Guth, Paul S. Effect of phenothiazines on neurohumor-containing particles from mammalian brain. *Federation Proceedings*, 1962, 21, 1100-1102.

Isolated nerve endings from guinea pig brain tissue (0.4-2.0 g) containing synaptic vesicles were treated with varying concentrations of chlorpromazine (5×10^{-5}) under several releasing procedures to determine the efficacy of chlorpromazine in preventing acetylcholine release from vesicular membranes. Parallel work involved acetylcholine release in isolated guinea pig ileum by 100°C at pH 4 followed by identification of the released neurohumor by destruction with acetylcholinesterase and alkaline blocking, atropine blocking and parallel assay procedures. With the isolated nerve ending preparations, chlorpromazine could not prevent release produced by incubation at 37°C or dilution to 0.032M sucrose. Chlorpromazine inhibited release more at 4-fold dilution than at 5-fold, and still more at 6-fold dilution. Graphic illustration of results indicates a curvilinear relationship between drug concentration and inhibition. Addition of exogenous acetylcholine indicated that the particles rejected the neurohumor. However, application of massive concentrations forced a small fraction of acetylcholine into the nerve endings, which is termed input rather than uptake. Chlorpromazine inhibits input almost as effectively as it inhibits release. The brain apparently does not contain a membrane which is selectively permeable to chlorpromazine; rather, certain brain areas are believed to concentrate the drug to a considerable extent.

Department of Pharmacology
Tulane University School of Medicine
New Orleans, La.

1958 Phillips, Barrie M., & Miya, Tom S. Excretion of S^{35} -prochlorperazine to rats subjected to experimental stress. Proceedings of the Society for Experimental Biology and Medicine, 1962, 109, 576-577.

Male Holtzman rats stressed for 12 hours by the bilateral hind leg ligation method according to Dexter et al. (1953), received $10/\mu\text{c}$ -175 g in an i.p. dose of 25 mg/kg prochlorperazine. They were placed in metabolism cages for 96 hours during which time urine and feces were collected. Rats subjected to experimental ligation excreted significantly smaller amounts of S^{35} in the urine following administration of S^{35} -prochlorperazine than did control animals. This

decreased excretion may be the result of diminished urine formation in stressed rats.

Department of Pharmacology
Purdue University
Lafayette, Ind.

1959 Gal, E. M., & Drewes, P. A. Studies on the metabolism of 5-hydroxytryptamine (serotonin). II. Effect of tryptophan deficiency in rats. Proceedings of the Society for Experimental Biology and Medicine, 1962, 110, 368-371.

Male Sprague-Dawley rats were divided into 4 groups; the 1st and 2nd groups were kept on tryptophan-sufficient diet with and without sulfasuxidine (10 g/kg), while the 3rd and 4th groups were on tryptophan-deficient diet with and without sulfasuxidine. The animals were fed these diets for a maximum of 6 weeks. Blood and weighed tissue samples were analyzed for 5HT content according to a modified method of Bogdanski et al. (1956). In some cases the animals were given a single i.p. injection of 1.86 mg/kg pheniprazine. Tryptophan-deficient rats showed significant decrease of 5HT in all their tissues analyzed. Feeding of sulfasuxidine, presumably through its antibacterial action, led to greater recovery of intestinal serotonin in tryptophan-deficient rats. Injection of pheniprazine resulted in a statistically significant increase of 5HT in the blood but not in the brain of deficient animals.

Department of Psychiatry
College of Medicine
State University of Iowa
Iowa City, Iowa

1960 Rosen, Lawrence, & Goodall, McC. Identification of vanillic acid as a catabolite of noradrenaline metabolism in the human. Proceedings of the Society for Experimental Biology and Medicine, 1962, 110, 767-769.

Four normal subjects were infused over a 1-hour period with $9.5 \mu\text{c}$ d,l-levarterenol- 2-C^{14} (d,l-noradrenaline- 2-C^{14} ; specific activity 20 mc/mM). Vanillic acid was identified as a urinary catabolite of levarterenol in man through column chromatography and scintillometric measurement. The ultimate formation of a small amount of vanillic acid from levarterenol involved

oxidative degradation of the side chain and therefore the most likely immediate precursor is 3-methoxy-4-hydroxymandelic acid. In a 24-hour period, vanillic acid accounted for 2.6% of the recovered C^{14} .

Memorial Research Center and Hospital
University of Tennessee
Knoxville, Tenn.

1961 Frank, Oscar, Baker, Herman, Ziffer, Herman, & Leevy, Carroll M. Metabolic lesions induced by thalidomide. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 875.

Thalidomide (0.1-10 mg/ml) was added to the nutrient medium in a protozoan test system using the photosynthetic flagellates *Ochromonas danica*, *Euglena gracilis*, *O. malhamensis*, and the ciliate *Tetrahymena pyriformis* to determine drug antimetabolite activity. Growth decreased in direct proportion to thalidomide concentration. The LD₅₀'s varied from 0.3-5.0 mg/ml, depending upon the organism. Growth inhibition was annulled by addition of nicotinic acid or nicotinamide, 1-10 mg/ml. None of the other B-complex vitamins reversed the inhibition. Amino acids, purines and pyrimidines alone or in combination were also ineffective. However addition of DPN or vitamin K reversed growth inhibition. Thalidomide apparently interferes with DPN synthesis or cytochrome reduction, and the resultant metabolic lesions affect cellular oxidation and may induce morphogenic aberrations. The protozoan test system constitutes an efficacious means for screening potentially toxic drugs.

[No address]

1962 Bernsohn, Joseph, Custod, James, Remenchik, Alexander P., & Talso, Peter J. Nucleotide metabolism in schizophrenia. *Journal of Laboratory & Clinical Medicine*, 1962, 60, 859-860.

Fresh erythrocytes from normal subjects, schizophrenic patients and nonpsychotic psychiatric patients were incubated with P^{32} for 20-120 minutes to compare the production of high energy phosphate bonds.

In order to determine the rate of P^{32} incorporation into adenine nucleotides, the following fractions were isolated: inorganic phosphorus, hexose diphosphate, ADP and ATP. The inorganic phosphorus levels rose in each group during incubation. Hexose diphosphate levels decreased moderately in normal patients and nonpsychotics, but rose slightly in schizophrenics. Adenosinediphosphate levels decreased significantly ($p < 0.001$) in schizophrenics, but remained constant in other groups. Schizophrenics show a reduced requirement for high energy phosphate bonds over a period of time.

[No address]

1963 Gardner, Thomas S., Wenis, Edward, & Lee, John. Monoamine oxidase inhibitors. III. Structural variations in 1-alkyl and 1-aralkyl-1 (or 2) acyl-hydrazines. *Journal of Medicinal and Pharmaceutical Chemistry*, 1962, 5, 503-513.

Modifications were made in iproniazid for the purpose of achieving a more specific distribution of the drug in various tissues. A number of sugar acyl, 4-hydroxybutyryl and D-pantoyl derivatives of benzylhydrazine, 4-dimethylaminobenzylhydrazine, and α -methylphenethylhydrazine were prepared by reaction of the corresponding lactones with the substituted hydrazines. The reaction product of D-ribonolactone with benzylhydrazine was shown to be a N^1, N^2 -hydrazine derivative. The most interesting compounds were 1-benzyl-2-(D-ribonoyl)hydrazine, and 1-benzyl-2-(D-pantoyl)hydrazine. The variation of the structures of active MAO inhibitors, such as 1-isopropyl-2-isonicotinoylhydrazine, 1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl)-hydrazine and 1-benzyl-2-picolinoylhydrazine, either eliminates or reduces MAO inhibitory activity. In one case, quaternization of 1-benzyl-2-picolinoylhydrazine with methyl iodide or methyl bromide increased response to 5HTP.

Hoffmann-La Roche Inc.
Nutley, N. J.

1964 Anton, Aaron H., & Sayre, David F. A study of the factors affecting the aluminum oxide trihydroxyindole procedure for the analysis of catecholamines. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 360-375.

A reliable quantitative method for catecholamine estimation in diverse biological material, mainly urine, from various vertebrate species is presented. It involves the selective adsorption of catecholamines onto a constant amount of aluminum hydroxide, elution with a constant volume of 0.05 N perchloric acid and measurement by the formation of fluorescent trihydroxyindole derivatives in the presence of potassium ferricyanide and 10 N alkali ascorbate. The relative fluorescence for 25 analogues of levarterenol are given.

Department of Psychiatry
University of Florida College of Medicine
Gainesville, Fla.

1965 Kopin, Irwin J., & Gordon, Edna K. Metabolism of norepinephrine- H^3 released by tyramine and reserpine. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 351-359.

In order to study the fate of levarterenol- H^3 (norepinephrine- H^3) released from binding sites by reserpine and tyramine, male Sprague-Dawley rats were given d, l-levarterenol-7- H^3 (100/ μ c in 2 ml saline) i.v. followed 10 hours later by either 4 i.v. doses of 10 mg/kg tyramine at 15 minute intervals or 2.5 mg/kg reserpine i.p. Also levarterenol- H^3 (1.0/ μ c) or normetanephrine- H^3 (1.0/ μ c) was slowly infused or injected in divided doses over a 1-hour period with 2.5 mg/kg reserpine or with 10 mg/kg tyramine in various schedules. As a result of tyramine administration, the bound catecholamines are released directly into the circulation; a small portion is metabolized in the tissue before release, predominantly by deamination; little levarterenol is released in an active form.

Laboratory of Clinical Science
NIMH
Bethesda, Md.

1966 Resnick, Robert H., Gray, Seymour J., Koch, James P., & Timberlake, William H. Serotonin metabolism in paralysis agitans. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 110, 77-79.

Metabolic observations in 10 cases of paralysis agitans and 12 control patients affected with other neurological diseases were conducted. The cases collected were free from liver dysfunction and azotemia, and were not receiving psychoactive drugs. In both groups endogenous 24-hour urinary excretion of 5HT and its major metabolic derivative 5HIAA were measured by standard techniques; these measurements were repeated following i.v. administration of 0.66 mg/kg 5HTP. Determination of total 5-hydroxyindole excretion by a modification of Udenfriend's procedure (1955) and paper chromatography were also carried out on urines collected following 5HTP infusion. The metabolism of 5-hydroxyindolic compounds in paralysis agitans is similar to that observed in other unselected neurological disorders. No clarification has yet been made in relation to the possibility that drug-induced extrapyramidal syndromes may be caused by 5HT deficiency.

Department of Medicine
Harvard Medical School
Cambridge, Mass.

1967 Carver, Michael J. Effects of sodium phenylpyruvate on brain amino acids. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 110, 171-173.

Brain slices from Sprague-Dawley rats were incubated in air with 0.01 mM glucose; 0.0018 mM sodium phenylpyruvate was added to the experimental Warburg flasks. The free amino acids were isolated from the tissue by the picric acid technique and chromatography. Addition of phenylpyruvate resulted in an increase in brain phenylalanine with a decrease in aspartic and glutamic acids, and glutamine. The concentration of other brain amino acids was unaffected.

Mental Retardation Clinical Research Center
Nebraska Psychiatric Institute
Omaha, Neb.

Blegdamshospitalet
Epidemisk afdeling
Blegdams, Denmark

1968 Eckhardt, Eileen T. & Plaa, Gabriel L. The effect of phenothiazine derivatives on the disappearance of sulfobromophthalein from mouse plasma. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 387-391.

Dye-disappearance curves were established in mice for sulfobromophthalein (BSP). Chlorpromazine, thioridazine or mercaptotiazinyl were administered orally in various doses to fasted mice, the phenothiazine derivative being given 2 hours before 15 mg/kg BSP. Dose-response studies, the duration of action and the effect of chronic treatment were investigated. A comparison between various phenothiazine derivatives (7 straight chain, 6 piperazine substitutions, 3 piperidyl substitution and 2 miscellaneous compounds—imipramine and phenothiazine) is also made. No residual alteration in hepatic function was observed after a 14-day treatment period. However tolerance developed to the dye retention phenomenon after 14 days of treatment. Probably the observed plasma dye retention is due to a decrease in hepatic blood flow.

Department of Pharmacology
University of Vermont College of Medicine
Burlington, Vt.

1969 Norredam, Kai. Transaminaseaktiviteten i serum efter indgift af morfin og pethidin. [Serum transaminase activity following administration of morphine and pethidine.] *Nordisk Medicin*, 1962, 67, 708-710.

SGOT and SGPT were assessed in 11 patients with varying symptomatology before and 3, 6, 12 and 24 hours after the s.c. administration of 14-20 mg morphine. In some cases examinations were made at 1 hour and 48 hours as well. After 1-3 days examinations were resumed with the administration of 75-100 mg pethidine s.c. In 2 out of 11 cases slight temporary rises in serum transaminase were found, but not at such levels as to justify a diagnosis of myocardial infarction.

1970 Eränkö, Olavi, Kokko, Aulikki, & Söderholm, Ulla. Starch electrophoretic separation of esterases in the adrenal medulla, adrenal cortex and the brain of the rat and the hamster. *Annales Medicinæ Experimentalis et Biologiae Fenniae*, 1962, 40, 146-161.

Extracts of rat and hamster brain, adrenal medulla and cortex were subjected to starch gel electrophoresis, according to the method of Markert and Hunter (1959). In all organs examined several reacting esterase bands were observed using the substrates α -naphthyl acetate, α -naphthyl butyrate, acetylthiocholine and butyrylthiocholine, alone or with an inhibitor such as eserine or 3 other compounds; inhibitor concentrations were usually 10^{-5} M. The bands differed from each other not only in electrophoretic mobility but also in regard to substrate and inhibitor characteristics. Carboic esterases appear to form a large family of enzymes, all members of which cannot be demonstrated with a single method.

Department of Anatomy
University of Helsinki
Helsinki, Finland

1971 Briggs, Michael H., Andrews, E. David, Kitto, G. Barrie, Segal, Leah, Graham, Venise, & Baillie, W. Jeavons. A comparison of the metabolism of ascorbic acid in schizophrenia, pregnancy and in normal subjects. *New Zealand Medical Journal*, 1962, 61, 555-558.

Urine samples collected from 15 male schizophrenic patients (mean age 40 years, mean duration of illness 12 years), 12 males with various psychoses (i.e., manic-depressive, senile mania, etc., mean age 44 years, mean duration of illness 7 years), 8 pregnant females (mean age 28 years), 9 normal females (mean age 31 years) and 16 normal males (mean age 29 years) were analyzed to determine the concentrations of ascorbate, dehydroascorbate and diketogulonate by a differential 2,4-dinitrophenol

method. Results indicated an impairment in ascorbate metabolism in schizophrenics, based primarily upon continual partial inhibition of p-hydroxyphenylpyruvate oxidase, which interferes with phenylalanine oxidase and results in engorgement of tissues with excessive aromatic compounds. In all groups, the total percentage of free ascorbic acid correlated with total metabolites about 0.1%. In order to minimize variations in ascorbic acid intake, 24-hour-urine samples were obtained from 8 pregnant females and analyzed for the above metabolites to determine whether or not increases in ceruloplasmin and plasma copper were related to excessive breakdown of ascorbic acid. Low urinary ascorbate metabolite values were found for both pregnant females and schizophrenics. This evidence may support the findings of Adelstein et al (1956) and others that a sharp rise occurs in ceruloplasmin and plasma copper during late pregnancy.

Victoria University of Wellington
Wellington, New Zealand

1972 Novák, I., Háznagy, A., & Szendrei, K. Beiträge zur UV-spektrophotometrischen Untersuchung und zu den "Beam-Chlorwerten" des ungarischen und indischen Hanfes. [Contributions to the UV-spectrophotometry and the "Beam chlorine values" of Hungarian and Indian hemp.] Pharmazie, 1962, 17, 294-297.

The previously established fact that Hungarian hemp contains only traces of physiologically active substances was confirmed by the results of a semi-quantitative modification of the Beam reaction in petroleum-ether extracts and by UV absorption curves. The size of the secondary absorption maximum provides a quantitative indication of the content of physiologically active substances, while the Beam chlorine values are only suitable for a qualitative judgment.

Institute of Pharmacognosy
Medical University
Szeged, Hungary

1973 Vecerkova, J., Sulcova, M., & KacI, K. Über den papierchromatographischen Nachweis der Antihistaminica und Atarac-

tica durch Umkehrphasenchromatographie im System Petroleum-Athanol/Wasser/Ammoniak. [The paper-chromatographic determination of antihistamines and tranquilizers by reversed-phase chromatography in the system petroleum-ethanol/water/ammonia.] Pharmazie, 1962, 17, 22-29.

Determination of the R_f -values of 24 antihistamines and tranquilizers (including 20 with a tertiary N and 4 with a quaternary N) in 5 solvent systems with a constant ammonia concentration (2%) and an ethanol concentration varying from 55 to 95% (descending chromatography at 12-15°C) showed that the mobility of compounds with a tertiary N increased with increasing ethanol concentration while that of quaternary compounds could be divided into 3 subgroups: 5 compounds in which there was a linear relationship between R_f -value and ethanol concentration, 9 compounds in which there was a more pronounced increase in R_f at lower ethanol concentrations, followed by leveling off, and 6 compounds which practically accompanied the solvent front. This system is therefore most useful for separating mixtures containing only 1 compound from each subgroup. A chart showing the color reactions of these compounds with H_2SO_4 , HNO_3 , $PdCl_2$, $FeCl_3$, $AuCl_3$, $Ce(SO_4)_2$ and Ehrlich's reagent is also presented.

Laboratory for Toxicology and Legal
Chemistry
Charles University
Prague, Czechoslovakia

1974 Klöcking, H.-P., & Walter, H. Über eine modifizierte Murexidreaktion zum qualitativen Nachweis von Barbitursäure- und Thiobarbitursäurederivaten. [A modified murexide reaction for the qualitative detection of barbituric acid and thiobarbituric acid derivatives.] Pharmazie, 1962, 17, 277-280.

Two simplifications of Handorf murexide reaction were used for the identification of barbiturates and thiobarbiturates in either pure form or commercial mixed preparations. The sensitivity thresholds of the 2 methods are given for 20 barbiturates and

thiobarbiturates, and the colors obtained in the dry residue or in ammonia are listed, along with the barbiturate content in %, for 22 commercial products. The sensitivity varies from 8-15 µg for most compounds to 30-100 µg for hexobarbital.

Pharmakologisches Institut
Universität Rostock
Rostock, Germany

1975 Klöcking, H.-P. Nachweis von Barbitursäurederivaten auf Papierchromatogrammen mittels der Chlor-Benzidin-Reaktion. [Detection of barbituric acid derivatives on paper chromatograms by means of the chlor-benzidine reaction.] *Pharmazie*, 1962, 17, 218-219.

A table illustrates the colors and sensitivity thresholds in the chlor-benzidine reaction for phenobarbital, barbital, allobarbital, 5-ethyl-5-crotyl-barbituric acid, propallylonal, cyclobarbital, methylphenobarbital, hexobarbital and aprobarbital following paper chromatography of 1% ethanol solutions in dimethylformamide/benzine-dioxane. This reaction, although not specific for barbiturates, may be useful under proper conditions.

Pharmakologisches Institut
Universität Rostock
Rostock, Germany

1976 Pfeifer, S. Gravimetrische Bestimmung des Morphins in Form einer Morphin-Molybdän-Vanadin-Verbindung. [Gravimetric determination of morphine in the form of a morphine-molybdenum-vanadium complex.] *Pharmazie*, 1962, 17, 128-133.

In a criticism of the paper by E. Kopp et al. (*Pharmazie* 17: 46, 1962), the author points out the deficiencies in their control studies and the fact that the optimal conditions established in preliminary experiments were not maintained in later work. He then reports studies of his own with varying concentrations of morphine and various mixtures of alkaloids, showing that the reproducibility of the method is very low (average error of -16.4 to +5.4%) and that the results are markedly affected by the presence of codeine, thebaine, narcotoline, narcotine or papaverine due to

coprecipitation (incomplete precipitation of other alkaloids by molybdate). The method is therefore usable only for a limited range of concentrations of pure morphine.

Pharmazeutisches Institut
Humboldt-Universität
Berlin, Germany

1977 Gonnard, Pierre. Effect of hydrazides and hydrazones of pyridoxal-5-phosphate on the cerebral glutamic decarboxylase and pyridoxal phosphokinase. *Acta Neurologica Scandinavica*, 1962, 38, 28-29.

Warburg manometric measurement of CO₂ output in cerebral glutamic acid decarboxylase of the rat, guinea pig and rabbit invariably demonstrates a deficiency of coenzyme in reference to the apoenzyme. Addition of pyridoxal phosphate greatly enhances CO₂ output. Pre-incubation of ATP pyridoxal and rabbit cerebral pyridoxal phosphokinase without preliminary incubation with glutamic decarboxylase and its substrate prevents phosphorylation of the pyridoxal. Although the pyridoxal phosphate hydrazones can function as coenzymes, the possibility of hydrazone hydrolysis releasing the pyridoxal phosphate during incubation must be discarded on the basis of evidence obtained by paper chromatography, the kinetics of the decarboxylation itself, and the lack of hydrolysis undergone by the hydrazone in pre-incubation studies. Therefore, the in vivo and in vitro pyridoxal phosphate deficiency induced by isoniazid cannot be attributed to a blocking of the coenzyme, for the above results confirm those formerly obtained with other pyridoxal enzymes. Other results indicate that addition of a small quantity of isoniazid to the pre-incubation medium completely inhibits pyridoxal phosphate formation without enhancing subsequent decarboxylation. Addition of isoniazid, decarboxylase and substrate after pre-incubation in no way inhibits decarboxylation.

Nouvelle Faculté de Médecine
45 Rue des Sts-Pères
Paris 6e, France

1978 Barron, Kevin D., Bernsohn, Joseph, & Hess, Adeline R. Electrophoretic

analysis of human brain esterases. *Acta Neurologica Scandinavica*, 1962, 38, Suppl. 1, 61-62.

Postmortem human brain esterases were studied by vertical starch gel electrophoresis of saline homogenates followed by application of histochemical staining techniques to the gel (zymogram). Enzymic activities of grey and white matter from the frontal, temporal, parietal, occipital and limbic lobes, telencephalic and diencephalic nuclei, brain stem and cerebellum were studied employing various esters of α -naphthol and β -naphthol, thioesterase iodides, chlorides, N-benzoyl-DL-arginine- β -naphthylamide (BANA) etc. as substrates. Enzyme activities have been surveyed over a pH range of 5.0-8.0 with determinations of susceptibility to fixation, aging and heat. Sixteen bands of nonspecific esterolytic activity occur against α -naphthyl acetate in normal white matter, while several additional bands occur with propionate and butyrate esters. Thioesterase resolves into 3 major bands. At least 4 zones of enzymic activity occur against BANA. Multiple bands of cholinesterase activity are also demonstrable and, in caudate-putamen, acetylcholinesterase activity resolves into 3 distinct zones. Nonspecific esterase and thioesterase are largely inhibited by cupric salts ($10^{-3}M$). Cholinesterase activities are eliminated by eserine ($10^{-5}M$) E 600 ($10^{-6}M$) TEPP ($10^{-6}M$) and DFP ($10^{-5}M$). Quantitative estimations of enzyme activities were made by reflection densitometry. Differences in substrate optima and inhibitor sensitivity have supported the concept that the numerous bands of activity shown by the varied staining techniques are due to specific molecular species of enzymes.

Neuropsychiatric Research Laboratory
VA Hospital
Hines, Ill.

1979 Carlsson, Arvid, Falck, Bengt, Hillarp, Nils-Ake, & Torp, Alf. Histochemical localization at the cellular level of hypothalamic noradrenaline. *Acta Physiologica Scandinavica*, 1962, 54, 385-386.

Catecholamines of the freeze-dried hypothalamus (mouse, rat, rabbit) were con-

densed with formaldehyde to highly fluorescent isoquinoline derivatives; serial sections were examined in a fluorescence microscope and then stained with toluidine blue. A rather intense yellow-green fluorescence develops in 3 circumscribed and bilaterally symmetrical areas within the hypothalamus: a large area in the preoptic region just ventrally and slightly dorsally to the anterior commissure with its largest extension in the lateral part; the supraoptic nuclei and the paraventricular nuclei. The fluorescent products are localized to very fine fibres running between and partially enclosing the nerve cells which themselves, like the glia cells, showed no fluorescence. The fibres, although finer, have the same characteristic appearance as the adrenergic nerve terminals in peripheral tissues, with small intensely fluorescent enlargements dispersed at irregular intervals. However they are not ordinary adrenergic nerves to blood vessels, as bilateral cervical sympathectomy does not cause them to disappear. The fibres probably represent synaptic terminals derived from brain neurons. The fluorescing substances are probably levarterenol (noradrenaline), dopamine and 5HT. Fluorescence disappears within 24 hours after the administration of 5 mg/kg reserpine s.c. to rats, and does not reappear for days. Administration of m-tyrosine in doses that deplete the hypothalamus of catecholamines but not 5HT also caused the fluorescence to disappear. Thus it appears that levarterenol in the hypothalamus is accumulated in what appears to be synaptic nerve terminals. Also there seems to be a local accumulation of levarterenol or possibly dopamine in the median eminence where the hypophyseal portal system arises.

Department of Pharmacology
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Göteborg, Sweden

1980 DeGiacomo, Piero. Histochemical research on some aspects of acetylcholinesterase and its inhibitors in the CNS. *Acta Neurologica Scandinavica*. 1962, 38, Suppl. 1, 55-56.

Gomori's method was used to determine the effect of certain reversible and irreversible inhibitors of cholinesterase on the CNS and

the distribution of acetylcholinesterase in the human CNS. Comparison of eserine, prostigmine and nivaline in guinea pigs and rabbits revealed that eserine induced a clearly visible blocking effect, while prostigmine exerted a slight, variable effect and the effects of nivaline were negligible. In vivo and in vitro experiments encompassed pre-treatment with reversible blocking agents of cholinesterase (eserine, prostigmine and nivaline) in comparison with the irreversible blocking action of diisopropylfluorophosphonate. In an attempt to demonstrate histochemically the different block levels between anatomical formation and another, the effects of progressive doses of diisopropylfluorophosphonate were investigated. Additional experiments included intracerebral and i.p. injections of Iso-OMPA and parathion. Nissl's histological method was also used. With respect to acetylcholinesterase distribution in the CNS, the neocortex exhibited lesser positivity than the paleocortex, and pyramidal cells were more positive than granular cells, the Betz cells (pyramidal) being most strongly positive.

Clinic of Nervous and Mental Diseases
Rome University
Rome, Italy

1981 Marshall, E. F., & Ansell, G. B. The effect of chlorpromazine on phosphate exchange in the phospholipids of rat brain in vivo and in vitro. *Acta Neurologica Scandinavica*, 1962, 38, 36-37.

Rat litter mates were subjected to chronic treatment with chlorpromazine (10 mg/kg/day) for a fortnight and maintained in a warm atmosphere with litter-mate controls. The capacity of the brain phospholipids to incorporate P 32 orthophosphate over a short exchange period was measured. There was a significant depression for phosphatidylcholine and phosphatidylinositol, but other alkali-labile phospholipids were unaffected. No effect was obtained on phosphorylethanolamine or phosphorylcholine. In in vitro experiments, brain cortex slices were incubated with 10^{-5} M chlorpromazine in glucose containing the medium. There was complete inhibition of P 32 orthophosphate uptake into the choline-, ethanolamine-, and serine-containing phospholipids, a 75% inhibition of

phosphatidylinositol uptake and no action on phosphatidic acid. Lower concentrations (10^{-4} M) however stimulated phosphate exchange in phosphatidic acid, had no effect on other phospholipids. Addition of ATP had no effect on chlorpromazine action. If the ATP was added 20 minutes before chlorpromazine, then the uptake into phosphatidic acid and phosphatidylinositol was partially restored to control levels though uptake into phosphatidylcholine and -ethanolamine was still completely inhibited.

Department of Experimental Neuropharmacology
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1982 Lagnado, J.R. Electrophoretic separation of rat brain esterases in starch gel medium. *Acta Neurologica Scandinavica*, 1962, 38, 63-64.

Electrophoresis of particle-free extracts of rat brain in starch gel medium resulted in the separation of 9-10 esterase bands as revealed by a technique similar to that of Hunter & Markert (1957). α -Naphthylacetate was used as a substrate. Cholinesterases were distinguished from other esterases by the use of neostigmine or eserine sulphate (10^{-5} M); acetylcholinesterases were specifically inhibited by 62 C 47 (10^{-5} M). E 600 (10^{-6} - 10^{-5} M) and p-chloromercuribenzoate (10^{-4} M) were employed to differentiate between arylesterases, carboxylesterases and C-esterases. Planimetry of the stained gel scans showed that cholinesterases (both types) contributed 45-55% of the total amount of developer deposited (naphthalene black 10 B); the remainder was contributed by arylesterases (ca. 35%), carboxylesterases (ca. 12%) and C-esterases (ca. 8%). Esterase zymograms obtained using extracts of newborn rat brains differed from those from adults in that carboxylesterase was virtually absent and the two arylesterases migrated more slowly.

Medical Research Council
Neuropsychiatric Research Unit
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See also 1680, 1690, 1692, 1715, 1718, 1754, 1762, 1808, 1886, 1910, 1911, 1912, 1930

ABBREVIATIONS

α -KG	α -ketoglutarate	HD	hypnotic dose
AACL	Zuckerman's Affect Adjustive Check List	5HIAA	5-hydroxyindoleacetic acid
ACTH	adrenocorticotrophic hormone	5HT	5-hydroxytryptamine
ad lib.	free choice	5HTP	5-hydroxytryptophane
ADP	adenosinediphosphate	i. a.	intraarterial
AM	morning	ibid.	in the same place
AMA	American Medical Association	i. e.	that is
Art.	Article	i. m.	intramuscular
ATP	adenosinetriphosphate	IMPS	Lorr's Inpatient Multidimensional Psychiatric Scale
BAL	British antiLewisite	i. p.	intraperitoneal
BAS	benzyl analogue of serotonin	IPAT	Cattell's Institute for Personality and Ability Testing Anxiety Scale
b. i. d.	twice a day	IQ	intelligence quotient
BOL	bromolysergic acid diethylamide	IU	international unit
BUN	blood urea nitrogen	i. v.	intravenous
ca.	about	kg	kilogram
CAR	conditioned avoidance response	K _i	Michaelis constant for an inhibitor
CBS	chronic brain syndrome	K _m	Michaelis constant for a substrate
cc	cubic centimeter	lbs	pounds
CDC	Communicable Disease Center	LD	lethal dose
cm ²	square centimeter	LSD	lysergide
cm ³	cubic centimeter	μ	micron
C. N. R. S.	Centre National de la Recherche Scientifique	μ c	microcurie
CNS	central nervous system	μ g	microgram
COMT	catechol-o-methyl transferase	μ l	microliter
cpm	counts per minute	μ M	micromolar
cps	counts per second	m	meter
CR	conditioned reflex(response)	M	molar
CS	conditioned stimulus	ma.	millamperes
CTD	climbing time delay	MACC	Motility Affect Cooperation Communication
DDT	dichlorodiphenyl trichlorethane	MAO	monoamine oxidase
DNA	deoxyribonucleic acid	MAS	Taylor Manifest Anxiety Scale
DOPA	3, 4-dihydroxy-phenylalanine	meq	milliequivalents
DPN	diphosphopyridinenucleotide	ml	milliliter
DPNH	reduced diphosphopyridine- nucleotide	mm	millimeter
ECG	electrocardiogram	mM	millimolar
Ed.	editor	mm ²	square millimeter
ED	effective dose	MMPI	Minnesota Multiphasic Personality Inventory
EDTA	ethylenediaminetetraacetic acid	MSRPP	Multidimensional Scale for Rating Psychiatric Patients
EEG	electroencephalogram	N	normal
e. g.	for example	NEFA	nonesterified fatty acid
ERG	electroretinogram	NIH	National Institutes of Health
et al.	and others	NIMH	National Institute of Mental Health
etc.	and so forth	p	probability
FFA	free fatty acid	PAH	para-aminohippuric acid
g	gram	PBI	protein-bound iodine
GABA	γ -aminobutyric acid		
GABOB	γ -amino- β -hydroxybutyric acid		

H	negative logarithm of hydrogen ion concentration	TD	toxic dose
PM	afternoon and evening	TH	thyroid hormone
o.	by mouth	t. i. d.	three times a day
pm	parts per million	TPN	triphosphopyridinenucleotide
PRP	Psychotic Reaction Profile	TPNH	reduced triphosphopyridine-nucleotide
		TSH	thyroid-stimulating hormone
i. d.	four times a day	U	unit
efs.	references	UR	unconditioned response
rf	ratio of the distance of dissolved substance to solvent distance	US	unconditioned stimulus
RNA	ribonucleic acid	USAF	United States Air Force
u	rat unit	USDHEW	United States Department of Health, Education, and Welfare
s. c.	subcutaneous	USP	United States Pharmacopoeia
S. D.	standard deviation	USPHS	United States Public Health Service
SGOT	serum glutamic oxaloacetic transaminase	UV	ultraviolet
SGPT	serum glutamic pyruvic transaminase	VA	Veterans Administration
ic	exactly as found	viz.	namely
SOSAI	Springfield Symptom and Adjustment Index	WAIA	Wechsler Adult Intelligence Scale
RA	Science Research Associates	WHO	World Health Organization
Suppl.	supplement	WPRS	Wechsler Psychiatric Rating Scale

AUTHOR INDEX

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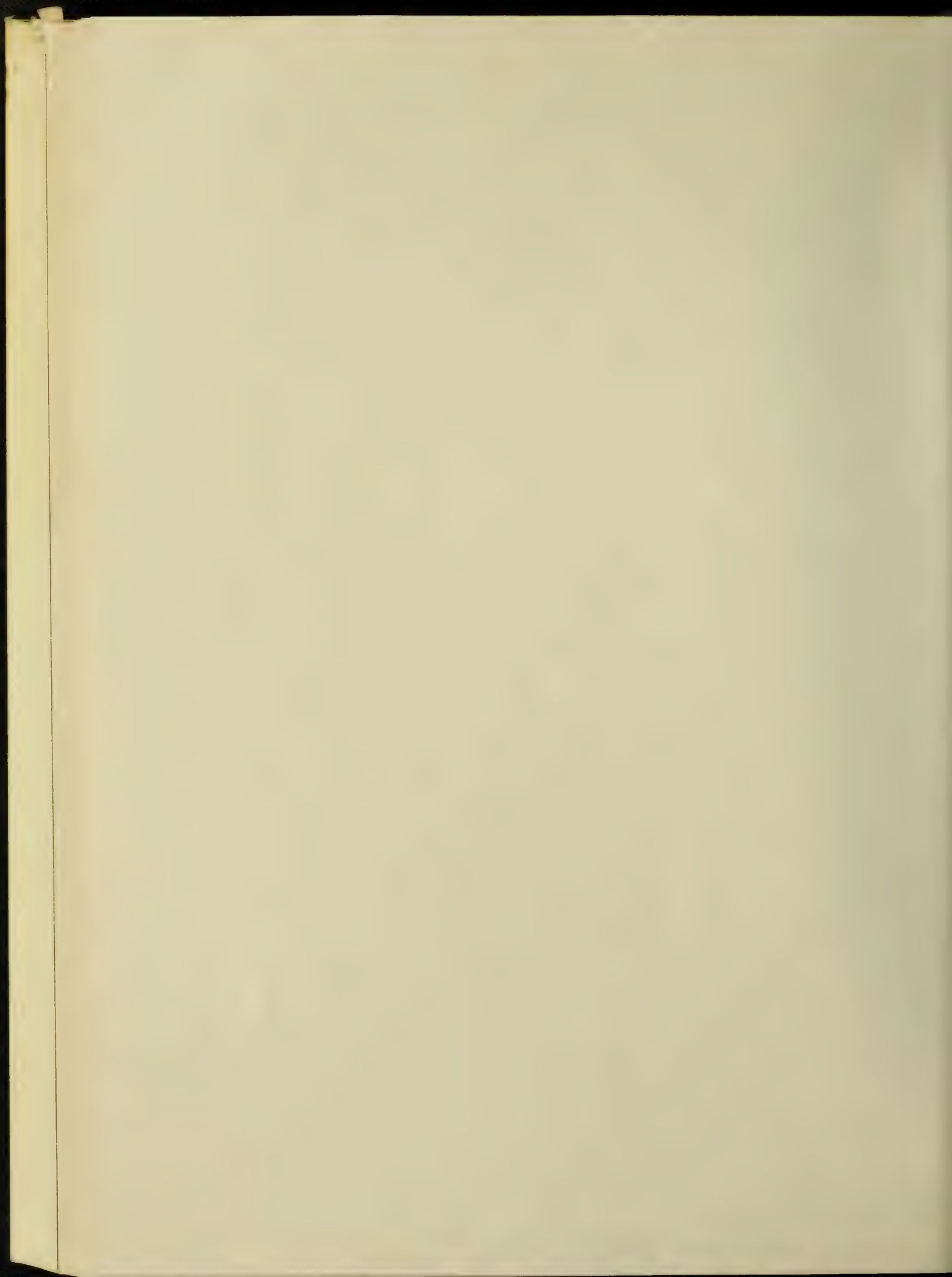
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Psychopharmacology
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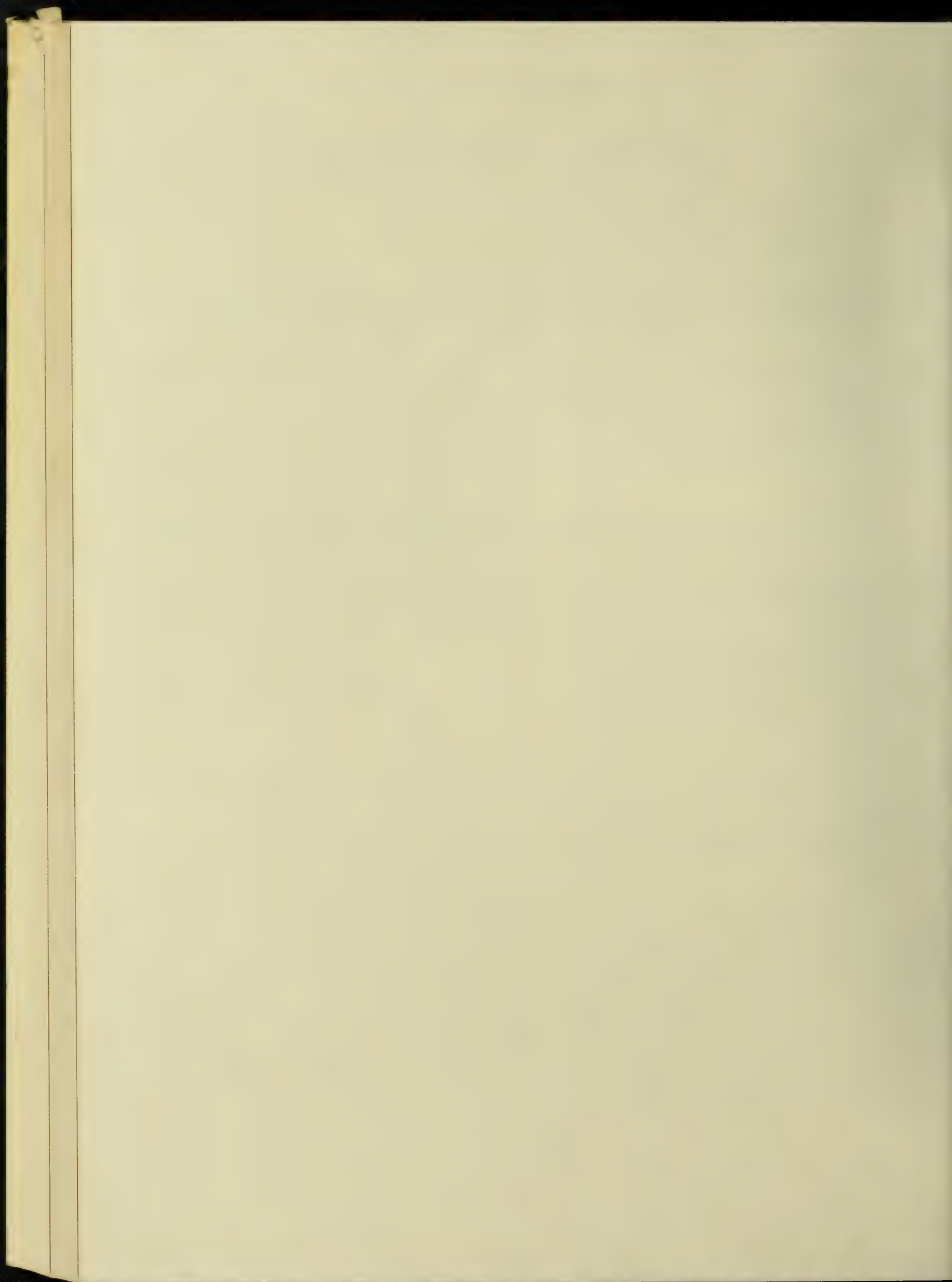
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Public Health Service
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Bethesda 14, Maryland

PSYCHOPHARMACOLOGY ABSTRACTS

Volume 2, Number 9

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REVIEWS, SUMMARIES, BIBLIOGRAPHIES,
GENERAL ARTICLES AND BOOKS

1983 Heinrich, K. Die Behandlung depressiver Angst- und Verstimmungszustände in der Praxis. [The treatment of depressive anxiety and mood disturbances in the general practice.] Fortschritte der Medizin, 1962, 26, 567-570.

The ambulatory treatment of hospital discharged patients suffering from depression, anxiety and mood disturbances is discussed. A guide is offered to the general practitioner regarding choice and dosage of psychopharmacological drugs and the duration of treatment. The drugs are divided into 3 groups: I Psycholeptic drugs, II Psychoanaleptic drugs, and III Ataractic drugs. Daily dosages are recommended, and side effects listed. (No refs.)

Universität-Nervenklinik
Mainz, Germany

1984 Stoerger, R. Zur neuroleptischen Behandlung endogener Psychosen. [The neuroleptic treatment of endogenous psychoses.] Medizinische Monatsschrift, 1962, 6, 155-158.

The development of psychopharmacology and psychochemotherapy since 1952 is reviewed in general terms, and its importance in the treatment of neurotic and psychotic disorders outlined and emphasized. (4 refs.)

No address]

1985 Elder, John T. Review of lysergic acid diethylamide (LSD) antagonists. Proceedings of the Western Pharmacology Society, 1962, 5, 35-41.

Drugs cited as antagonists to LSD include: nicotinic, glutamic and succinic acids, histamine, various steroids, tranquilizers including meprobamate, chlorpromazine and reserpine, barbiturates and autonomic drugs such as atropine and scopolamine. According to the results of antagonism studies, the premise may be taken that LSD mimicked 5HT in producing most of its CNS effects. However the lack of activity of some 5HT antagonists such as atropine, and a serotonin-depleting agent such as

reserpine casts some doubt on this premise. Possible mechanisms of action and the possibilities of reciprocal relationships are discussed. (83 refs.)

Department of Pharmacology
University of Washington Medical School
Seattle, Wash.

1986 Harney, Malachi L. Current provisions and practices in the United States of America relating to the commitment of opiate addicts. Bulletin on Narcotics, 1962, 14, 11-24.

The history of narcotic addiction in the USA, its characteristics, the necessity for added control, the federal narcotic hospitals (Lexington, Ky. and Fort Worth, Tex.) and their contributions, the series of opiate addiction treatments, the New York, California, Michigan and Illinois programs, other programs, arguments pro and con compulsory treatment, and particularly emphasis on the use of nalorphine in the detection and attempted control of addicts are reviewed. A small dose of nalorphine (3 mg) will promptly produce enlargements of the pupils in opiate usage, the change depending to some extent on the degree of dependence to the opiate. Yet this dose is small enough so that severe and disagreeable withdrawal symptoms are not produced. Nalorphine programs have substantially contributed toward reducing the incidences of relapses to narcotics by addicts and have enabled authorities to detect very quickly those who do relapse before serious addiction can be resumed. (No refs.)

[No address]

1987 Bulletin on Narcotics. Estimated world requirements of narcotic drugs in 1962. Bulletin on Narcotics, 1962, 14, 47-48. [Editorial]

The Drug Supervisory Body of the United Nations publishes an annual statement of estimated world requirements for 60 narcotic drugs which enabled the Permanent Central Opium Board to calculate manufacture and import limits on these drugs for 116 countries and 64 nonmetropolitan

Reviews
Abstracts 1988-1992

territories for the forthcoming year. Consumption figures on the 60 narcotics are given for 1956-1962. (No refs.)

United Nations
New York, N.Y.

1988 Public Health Reports. Thalidomide. Public Health Reports, 1962, 77, 946. [Editorial]

A survey of 1,258 physicians in the USA interviewed by the FDA revealed that 20,771 patients received thalidomide, of which 3,879 were women of child-bearing age and 624 were pregnant. Most had not delivered and 9 cases of abnormality have been reported in offspring of patients who took thalidomide. Thalidomide was definitely not at fault in 1 instance, but 8 cases remain under investigation. Most of the physicians reported that they received admonitions from the manufacturer to discontinue thalidomide administration, but 85 stated that they were not warned of adverse drug reactions and 42 received no communication from the manufacturer. Thalidomide may still be found in medicine cabinets in the United States. (14 refs.)

Superintendent of Documents
Government Printing Office
Washington 25, D.C.

1989 Current Medical Digest. Emotional disorders of menopause. Current Medical Digest, 1962, 23, 139-142. [Editorial]

Caldwell (1961) administered thioridazine to 150 women with menopausal symptoms. Anxiety, tension and depression were markedly improved in all patients. Drowsiness, the only side effect, was rectified by decreasing drug dosage. Oral estrogens were required as adjunctive therapy in 30 patients to control hot flashes and night sweats. Another 40 found that thioridazine controlled these symptoms, while the remaining 20 required brief intermittent therapy with stilbestrol. Reassurance and a thorough explanation of menopausal symptoms does much toward restoring the confidence of these patients. (1 ref.)

Williams & Wilkins Company
428 E. Preston St.
Baltimore 2, Md.

1990 Michel-Wolf fromm, H. A propos des indications de la psychopharmacie en gynécologie. [The indications of psychopharmacy in gynecology.] Acta Psychosomatica, 1962, 10, 75. [Abstract]

There are 4 major indications for psychoactive drugs in gynecology: premenstrual disorders, hormonal imbalances, premenstrual pause and the consequences of physical or psychic traumas. Drugs should be specifically prescribed, however at the present time unsatisfactory empirical compromises are made. (No refs.)

[No address]

1991 Helwig, H. Thalidomid-Embryopathie. Bericht über die Jahrestagung der Nordwestdeutschen Gesellschaft für Kinderheilkunde in Hamburg vom 27.-29. April 1962. [Thalidomide-Embryopathy. Proceedings of the annual meeting of the Nordwestdeutsche Gesellschaft für Kinderheilkunde in Hamburg, April 27-29, 1962.] Fortschritte der Medizin, 1962, 80, 471-472.

Sixteen out of 20 papers presented at a pediatrics conference in Hamburg were concerned with the effects of thalidomide on the human or animal embryo; the remaining papers dealt with immunization and nutrition of the infant. (20 refs.)

[No address]

1992 Deisher, Robert W., Balkany, Andrew F., Prewitt, Charles D., & Redfield, William J. Phenylketonuric families in Washington State. American Journal of Diseases of Children, 1962, 103, 818-821.

A list of all known cases of phenylketonuria within the state of Washington was compiled from various institutions for retarded children and from private physicians

having phenylketonurics as patients. A total of 41 homes was visited, questionnaires were completed by investigators and all preschool children were tested for phenylketonuria by both the ferric chloride and the Phenistix tests. There are 61 known cases of phenylketonuria in the state of Washington, slightly more than 80% of which reside in state mental institutions. These children appeared normal at birth, and the disease was not manifested until the child was 6 months to 2 years of age. More than 80% were blond with fair complexions, 26% had convulsions and 29% had eczema. Parents were informed of the importance of early dietary management to prevent mental retardation. A register of these families was established and is being operated by the Washington Department of Health. (4 refs.)

University of Washington School of Medicine
Seattle, Wash.

1993 Sattes, Hans. Zur Anthropologie der Drogenabhängigkeit. [Anthropology of drug addiction.] *Nervenarzt*, 1962, 33, 184-187.

The potential addict is a person lacking purpose in life, who feels lost and captive in his environment and is likely to acquire purposeless habits in order to fill his inner vacuum. Experience with narcotic drugs produces an exciting emotional experience which rapidly leads to addiction. A successful cure is possible only if the addicted person gains insight, and acquires the ability and desire to change his personality. This high degree of essential cooperation accounts for the poor therapeutic prognosis. (5 refs.)

Universitäts-Nervenklinik Würzburg
Würzburg, Germany

1994 Stubblefield, R.L. The impact of tranquilizing drugs regarding medical practice. *Dallas Medical Journal*, 1962, 48, 276-277.

The following tenets are designed to facilitate the physician's wise recommendation of tranquilizing drugs: accurate diagnosis of the patient's biological state, careful judging of his interpersonal, intrapsychic, external stress situations, careful judging of the doc-

tor-patient relationship, assessment of the patient's allergic and toxic history of susceptibility to drugs and regular evaluation of biological state of the patient plus a thorough study of few drugs in clinical trials. The psychoactive drugs may be utilized to improve the doctor-patient relationship by providing symptomatic relief and reduction in the patient's anxiety-hostility responses.

Dallas Medical Journal
Dallas, Tex.

1995 Groh, Ch. Therapie der Epilepsie im Kindesalter. [The therapy of epilepsy in childhood.] *Monatsschrift für Kinderheilkunde*, 1962, 110, 96-103.

The development of the chemotherapy of epilepsy over the last 100 years is briefly reviewed; a table lists the predominant types of epilepsy, the drugs recommended and the daily oral dosage according to age groups. Treatment with anticonvulsants is still regarded as the main pillar of treatment. The psychopharmaca (the "non-specific" drugs) which influence the general condition of the patient are also considered important, as are general hygienic and dietetic measures, and psychologic and pedagogic guidance of the patient in his environment. Therapy with ACTH and cortisone-derivatives, which was initiated in 1958, especially for "propulsive petit mal" in infants, has brought about a decisive change in management. Different types of side effects are discussed; side effects affecting the CNS often are signs of overdosage. This is true also for damage to the hematopoietic system, as well as damage to the liver or kidneys. The necessity of checking the EEG and blood count regularly is emphasized. The gradual reduction in the dosage of anticonvulsive drugs throughout at least 1.5-2 years is stressed, especially during puberty.

Universitäts-Kinderklinik
Vienna, Austria

See also 2057, 2105

CLINICAL STUDIES

1996 Wrede, Josef. Beitrag zur medikamentösen Behandlung von Angst- und Zwangsvorstellungen. [Contribution to the chemotherapy of anxiety and compulsive obsessions.] Therapie der Gegenwart, 1961, 100, 568-570.

Thirty-seven patients were treated with chlordiazepoxide (Librium). The maximal dose was 10 mg t.i.d. The patients were suffering from anxiety in varying degree, compulsive obsessions, phobias and slight depressions coupled with fear. No side effects were noted during 2-3 months of treatment except in 1 case. All patients whose anxieties and phobias were not of psychotic origin were greatly improved. Far-reaching insight by the patient into his own problem could often be achieved.

Krankenhaus für Nerven- und Gemütsleiden
Rottenmünster bei Rottweil
Rottweil, Germany

1997 Wieck, H.H., Brilmayer, H., & Picka, N. Durchgangs-Syndrome infolge von Vergiftungen mit Barbituraten. [Temporary degeneration syndromes following barbiturate intoxications.] Neurologie, Psychiatrie, Neurochirurgie, 1962, 30, 304-324.

The reversible psychic degeneration syndrome which occurs when overdoses of barbiturates are taken was measured in 141 patients and related to barbiturate blood concentrations. Measurements of the severity of the syndrome were obtained by calculating the Böcker test score, which combines in a single figure the reaction and resolution times and number of errors made in the solution of a series of problems involving recognition, recall, color differentiation, ordering ability, verbal reproduction and nonverbal contact receptivity. The general time sequence pattern in severe intoxications is (1) unconsciousness, (2) complete mental and physical confusion, (3) severe degenerative syndrome, (4) moderate syndrome and (5) mild syndrome. In the case history reported here as typical of such conditions, the duration of the above states was 2, 3, 2, 1, 1 and 7 days, corresponding to barbiturate concentrations in the patient's serum which declined from a maximum of about

16 mg% to 1.0 mg% on the 10th day, and to 0.5 mg% on the 14th day. Similar but less exhaustive tests on 45 other cases indicate that the barbiturate concentration in the serum bears a definite relation to the severity of symptoms; the curve for the latter seems to lag behind that of the former.

Universitäts Nervenklinik Köln
Cologne, Germany

1998 Scharff, O., & Stöger, R. Zur Hypertoniebehandlung mit Iproniazid (Marsilid). [Treatment of hypertension with iproniazid (Marsilid).] Medizinische Welt, 1962, 15, 826-830.

Thirty-six hospitalized and 38 ambulatory patients with hypertension were treated with iproniazid (Marsilid). The majority of patients were over 60 years of age. In order to facilitate the evaluation of the hypotensive effect of iproniazid, the hospitalized patients were pretreated with bed-rest, diet and medication for 1-3 weeks, until stabilization of the blood pressure was achieved. The dosage was in most cases 25 mg 3-5 times a day. The effect of the therapy became evident after 2-3 weeks. From that point on the dosage was reduced to 25 mg b.i.d. or t.i.d. Repeated examinations of urine and blood did not show any pathological changes. Various liver function tests did not reveal any liver damage. Iproniazid was generally well tolerated and achieved, in 65-70% of the patients, a distinct reduction of blood pressure. In addition, improvement of subjective complaints could be noted in 50-60% of the patients. Iproniazid was not well tolerated by hyperesthetic patients who reacted with much increased restlessness and a multitude of functional disturbances. In view of the stimulating effect of iproniazid, it is recommended to give the last daily dose not after 5 p.m. After discontinuance of the treatment, the blood pressure remains lowered for 10 days to 5 weeks.

Internen Abteilung des Krankenhauses
der Barmherzigen Brüder
Vienna, Austria

1999 Simpson, B.R., Seelye, Eve, Clayton, J.I., & Parkhouse, J. Morphine combined with tetrahydroaminacrine for postoperative pain. *British Journal of Anaesthesiology*, 1962, 34, 95-101.

Ninety-two surgical patients were treated; 40 received morphine alone (e.g., 15 mg) and 52 morphine with tetrahydroaminacrine (THA). The standard doses were compared with double doses combined with THA (20-30 mg) for the treatment of pain following abdominal and perineal surgery. Patients were assessed not only according to the amount of pain before and after treatment but also according to their level of consciousness, ability to move and willingness to cough. An improvement was achieved in the level of consciousness using THA, but no obvious improvement in pain relief, movement of coughing from the combination was obtained with the larger doses of morphine, i.e., although patients were more alert after THA, they were not markedly better off in other ways.

London Hospital
London, Great Britain

2000 Trent, Chester L. Changes in the Clyde Mood Scale produced by a sleep threshold dose of amobarbital. *Psychopharmacologia*, 1962, 3, 468-472.

Twenty-six psychiatric patients (depressive reaction, obsessive compulsive, conversion, schizophrenic, manic depressive, etc.) aged 15-61 years, received amobarbital (median dose in 20, 6 mg/kg i.v. infusion; median dose in 6, 10 mg/kg i.v. infusion) in conjunction with the Clyde Mood Scale and a mechanical technique for determining sleep threshold in order to investigate the relationship between the amount of amobarbital required to achieve the sleep threshold and to evaluate the affective state of the subject at the time of drug administration. No relationships were observed between the initial Clyde Mood Scale sub-scale scores and the sleep threshold dose for amobarbital. The only significant changes in the Clyde Mood Scale were reductions in the jittery sub-scale. The median dose of amobarbital required

to achieve sleep threshold in this study (6.0 mg/kg) was remarkably close to that (6.1 mg/kg) determined in a study by Shagass (1958).

Department of Psychiatry
University of California School of Medicine
San Francisco, Calif.

2001 Goldman, Douglas, & Rosenberg, Brigitte. Electro-encephalographic observations in psychotic children. *Comprehensive Psychiatry*, 1962, 3, 93-112.

Over a period of 1-10 years, social studies, physical and mental status examinations, various psychological tests and EEG observations were performed on 132 hospitalized, psychotic children, aged 6-13 years, (35 CBS, 31 schizophrenic, 52 personality disorders, 7 mentally deficient and 7 miscellaneous cases). A normal EEG was rare among these mentally disturbed children. The effect of small, sub-anesthetic doses (25-75 mg i.v.) of pentothal during the EEG was studied, and a correlation with the nature of the illness was established (i.e., in schizophrenic functioning), but residual inconsistencies occurred chiefly in patients with personality disorders. Prochlorperazine and Win-13, 645-5 [dosages unspecified] were used to indicate a correlation between EEG and clinical improvement.

Department of Psychiatry
Good Samaritan Hospital
Cincinnati, Ohio

2002 Boatman, Maleta, & Berlin, I.N. Some implications of incidental experiences with psychopharmacologic drugs in a children's psychotherapeutic program. *Journal of Child Psychiatry*, 1962, 1, 431-442.

Eighteen children, aged 2 1/2-21 years, exhibiting hyperactivity and aggressive behavior (1 phobic, 13 psychotic, primarily schizophrenic, 3 epileptic and 1 with borderline intelligence) were treated with tranquilizers. Nine were analyzed in case history form. They received psychotherapy and various psychoactive drugs, including reserpine (0.1-0.3 mg t.i.d.), chlorpro-

mazine (20 mg/day-200 mg q.i.d.), diphenylhydantoin, meprobamate (400 mg t.i.d. or every 4 hours) and prochlorperazine (60 mg per day). Medication was clearly helpful to 6 and largely detrimental to 4 children. The 6 clearly showed reduction of excited, aggressive and destructive behavior. For 2 of these, however, onset of behavioral alterations was too rapid to be credited to drug action, and for the rest, the behavioral changes that occurred seemed related to the psychological climate surrounding the prescription and administration of the drugs. For the same 6 children similar changes in behavior were also noted during psychotherapy without medication. In the other 12 out of 18 children, no clear behavioral changes were noted. There were psychological factors which may have contributed to chemotherapeutic failure. As the psychological circumstances involved in the prescription and administration of psychopharmacological drugs may be of importance in evaluating their efficacy, such data should more frequently be included in reports on these drugs.

Children's Service
Langley Porter Neuropsychiatric Institute
San Francisco, Calif.

2003 Diethelm, Oskar, & Barr, Rosalie M. Experimental study of amnestic periods in acute alcohol intoxication. *Psychiatria et Neurologia*, 1962, 144, 5-14.

Fifteen severe alcoholics, aged 22-48 years, received ethanol (75-100 cc in 450-500 cc of saline i.v.) infusions over an 18-22 minute time span, after and during which all conversation was recorded on tape for 45 minutes in order to determine the occurrence of amnestic episodes. All patients exhibited alcoholism related to an ill-defined psychoneurotic illness or anxiety reaction. The observer asked the patient to describe all details which he could remember 24 hours after the infusion. When amnesia occurred, the patient was permitted to listen to a recording of the incidents in question. Amnestic episodes were of short duration and contained psychologically meaningful material which would have been unpleasant for the patient to remember. Most patients felt intoxicated

during the actual infusion, but were well coordinated in thinking and speech. Amnestic periods of 10-20 minutes occurred in 3 severely psychoneurotic patients. These episodes were accompanied by unusually high blood ethanol levels and toxicity may well have been an important factor.

Department of Psychiatry
Cornell University Medical College
Ithaca, N.Y.

2004 Dyrberg, V. Haloperidol (Serenase) in the prevention of postoperative nausea and vomiting. *Acta Anesthesiologica Scandinavica*, 1962, 6, 37-47.

In a double-blind study, 548 surgical patients, 17-75 years of age, received haloperidol (5 mg i.v.) during the 1st part of standard anesthesia, while placebo was given to 541 patients to determine the postoperative antiemetic properties of haloperidol. Degree of nausea was determined by interviews 6 and 24 hours postoperatively and instances of vomiting were recorded. Compared to placebo haloperidol reduced postoperative nausea from 28.6% to 7.6% in males and from 49.5% to 20.3% in females for 18 hours postoperatively. Results in the control group indicated no relationship between nausea and the patient's age or duration of anesthesia, but a higher overall incidence of postoperative nausea and vomiting occurred in women than in men, particularly in relation to area of abdominal surgery. To compare results of haloperidol, placebo and chlorpromazine in women who had all undergone abdominal hysterectomy under the same conditions, 114 patients from the present series who had received 15 mg haloperidol were compared with 2 groups from a previous study: 159 who had 10 mg morphine and 158 who had received 50 mg chlorpromazine as premedication. All patients given haloperidol had complete amnesia for the anesthesia, while only 6 chlorpromazine and 7 control patients were amnestic. Haloperidol was a more active antiemetic than chlorpromazine, reducing the incidence of reflex movements during light anesthesia. While the postoperative incidence of nausea and vomiting is not great enough to justify routine

use of an antiemetic, in cases of established postoperative vomiting or for prophylaxis in special circumstances, haloperidol is recommended.

Department of Anesthesia
Copenhagen County Hospital in Gentofte
Hellerup, Denmark

2005 Bonica, John J., Green, Henry D., Dixon, H. Loring, Goodson, David N., Rensaa, Margaret A., & Sell, Irl T. Clinical evaluation of fluphenazine dihydrochloride as antiemetic agent. *Anesthesia and Analgesia*, 1962, 41, 732-739.

In a double-blind study designed to evaluate the postoperative antiemetic properties of fluphenazine, 4 groups of patients undergoing general anesthesia, including 1 group from each of 3 hospitals (497, 341 and 356 patients respectively) and 1 group of 143 obstetric patients, were used to determine the most effective drug dose and route of administration. Each of the 4 groups was divided into a placebo group and 4 subgroups who received the following dosage schedules: 1 hour prior to termination of anesthesia, fluphenazine (1.5 mg i.m.) was administered to group I and II and 2.5 mg i.m. was administered to group III. Ten minutes before termination of anesthesia, fluphenazine (1.0 mg i.v.) was administered to group II and 2.5 mg was administered i.v. to group IV. The most effective dosage was 2.5 mg administered i.v. about 10 minutes before the termination of anesthesia, which reduced the incidence of emetic symptoms from 44.4% to 9.3%. The incidence of hypotension and extrapyramidal reaction was low and sleeping time after the termination of anesthesia was not prolonged. Each patient was observed constantly for emetic signs and symptoms during the 1st 4 postanesthetic hours. Patients who received fluphenazine benefited to a highly significant degree. Fluphenazine is obviously one of the better antiemetics currently available.

Department of Anesthesiology
University of Washington
Seattle, Wash.

2006 Fisher, G.W., Murray, F., Walley, M.R., & Kiloh, L.G. A controlled trial of imipramine in the treatment of nocturnal enuresis in mentally subnormal patients. *American Journal of Mental Deficiency*, 1962, 67, 536-538.

Thirty-four mentally subnormal or severely subnormal epileptics with nocturnal enuresis, aged 7-67 years, were divided into 2 groups and given imipramine (25-50 mg per day) or inert placebo alternated on a double-blind basis for 8 weeks, preceded by 4 weeks during which frequency of "wet nights" was determined. Aside from the epileptics, all patients exhibited a tendency toward somewhat fewer episodes of enuresis with imipramine than with placebo. These differences were not statistically significant. Imipramine is apparently ineffective in controlling enuresis, at least at the dosages employed.

Prudhoe and Monkton Hospital
Prudhoe-on-Tyne, Northumberland
Great Britain

2007 Vyas, K.J. Hydroxyzine hydrochloride in paediatrics. *Antiseptic*, 1962, 59, 877-878.

Hydroxyzine drops (2-7 drops b.i.d. or t.i.d.) were administered to 60 children aged 1-18 months (22 with evening colic, 10 with abdominal colic, 8 with acute diarrhea and 20 with acute upper respiratory tract infections). Results were excellent in 54 children and good in 6. Effects were palliative, and the drug's antihistaminic property was beneficial in the respiratory tract infections. Crying children were promptly pacified after drug administration. The drops were given for 1.5-2.0 months to 2 infants who cried persistently, and improvement was promptly sustained. No toxic effects were observed.

Children's Ward
General Hospital
Junagadh, India

2008 Chatterji, N.N. Psychopharmacology of phenothiazine. *Antiseptic*, 1962, 59, 120-124.

Chlorpromazine [dosage unspecified] was administered to 364 patients (112 schizophrenics, 25 paranoids with systematized delusions, 65 manic-depressives and 75 psychoneurotics). Trifluopromazine [dosage unspecified] was administered to 64 patients (40 schizophrenics and 24 manic-depressives). Prochlorperazine (75-125 mg per day) was given to 68 patients (40 chronic schizophrenics and 28 with acute manic states). Trifluoperazine [dosage unspecified] was given to 100 schizophrenics. Thioridazine (75-400 mg per day for 3-4 months) was administered to 30 schizophrenics. Chlorpromazine was particularly effective in catatonic schizophrenia, offering amelioration of symptoms like mutism, catatonic stupor and cerea flexibilitas. Results with trifluopromazine were optimal in the paranoid group, obliterating delusions and hallucinations. Prochlorperazine was most efficacious in chronic schizophrenia, particularly the paranoid variety, and was superior to chlorpromazine in allaying excitement. Trifluoperazine was very effective in paranoid schizophrenia and catatonic states but its action in other psychoses was most discouraging. Paranoid schizophrenics with prominent hallucinations responded best to thioridazine. The postulated mechanism of action for the phenothiazine tranquilizers involves direct action on the hypothalamic stores of bound levarterenol and serotonin which in turn precipitate alterations in the patient's psyche.

Lumbinipark Mental Hospital
Calcutta, India

2009 Lamphier, Timothy A., Chin, Stanley, Crooker, Lester, Arthurs, Alexander, & Goldberg, Ronald I. Chlordiazepoxide as a preoperative and postoperative medication. *Clinical Medicine*, 1962, 69, 2466-2469.

Chlordiazepoxide (30-80 mg/day p.o. or i.m.) was administered as presurgical adjunctive medication to 287 anxious patients, aged 9-78 years, from 1-4 days preoperatively and 50-80 mg i.m. q.i.d. was continued postoperatively. Inert placebo was administered to 56 patients who served as controls. To ascertain the feasibility of this study, 35 patients also received

chlordiazepoxide (10 mg p.o., b.i.d.) for 1-4 days preoperatively. Adequate tranquilization was obtained in 29. Psychic status (anxiety, cooperativeness and mood) was evaluated by the doctor and nurses before and after medication. Of 287 patients, 274 were less apprehensive about the impending operation, manifesting increased cooperation with definite mood elevation. Excellent results were obtained in 178 patients, good results in 80, fair results in 17 and poor results in 12. Amelioration of anxiety began after the 1st dose. Only 2 of the 56 patients receiving placebo showed improvement. Of those achieving poor results, 12 developed nausea and vomiting after 4 days of therapy, and discontinuation of treatment resulted in recovery. Chlordiazepoxide was particularly useful in cases where tension and anxiety were associated with symptoms derived from organic pathological changes.

[No address]

2010 Hyman, Yvette K., & Orkin, Louis R. Triflupromazine and fluphenazine as adjuncts in anesthetic management. *New York State Journal of Medicine*, 1962, 62, 480-485.

To determine sedative, hypnotic and antiemetic properties, triflupromazine (2-6 mg i.m.) and fluphenazine (2-6 mg i.m.) were administered to 24 patients scheduled for ECT. Thiopental was administered alone and in combination with triflupromazine or fluphenazine in a series of trials with an interval of at least 3 days between each trial. Fluphenazine reduced the thiopental requirements from 5-30%. Triflupromazine reduced thiopental requirements from 15.5-58.9%. Both triflupromazine and fluphenazine (6 mg dose) had approximately the same sedative potency as 50 mg of pentobarbital. In a study of preoperative medication effects on 160 patients, aged 12-60 years, 10-20 mg triflupromazine administered i.m. 1 hour preoperatively, alone or with scopolamine, produced good sedation. Fluphenazine at 4-6 mg tranquilized effectively, but induced little sedation. In 28 patients who were scheduled for bronchspirometry or bronchoscopy under topical anesthesia, triflupromazine was very useful in relieving

apprehension. In a group of patients under spinal or peridural anesthesia marked hypotension was frequently seen with 2 mg doses of triflupromazine. When both drugs were administered to 60 patients with a history of nausea in surgical procedures of the head and face, fluphenazine was a more effective antiemetic than triflupromazine, with smaller dosage requirements. Both drugs were effective in treating emergence delirium, although fluphenazine is preferred because it does not prolong the anesthesia time. Triflupromazine potentiated the general anesthetic effect but fluphenazine did not. The use of these drugs in spinal anesthesia is contraindicated but further study should be made of triflupromazine as a sedative and fluphenazine as an antiemetic.

Department of Anesthesiology
Bronx Municipal Hospital Center
Bronx, N.Y.

2011 Sheiner, Ben. Triflupromazine hydrochloride (Vesprin) in pediatric premedication for tonsillectomies. *Anesthesia and Analgesia*, 1962, 41, 697-699.

Triflupromazine (5 mg/15 pounds) and pentobarbital (25 mg/15 pounds) were administered to 60 children as premedication for tonsillectomy while 45 children received pentobarbital (25 mg/15 pounds) and scopolamine (0.1 mg/15 pounds) as premedication 90 minutes before initiation of anesthesia. Of those who received triflupromazine, 49 were sleeping upon entry into the operating room, while only 25 who received scopolamine were asleep. Triflupromazine treated children remained asleep postoperatively for several hours and only 20% had any postoperative nausea and vomiting, while those on scopolamine awoke more rapidly and 61% experienced nausea or vomiting. More narcotic drugs were required by children treated with scopolamine. Overall, triflupromazine produced a 27% increase in the percentage of patients entering the operating room asleep, decreased postoperative nausea and vomiting from 61% to 20% and decreased the number of children requiring postoperative narcotics from 65% to 10%. Chi square analysis of resultant statistical data yielded corroboration of the above observations.

Department of Anesthesia
Pascack Valley Hospital
Westwood, N.J.

2012 Krawiec, Jaime S., Desiderio, Vincent, Bodi, Tibor, & Gambescia, Joseph M. Effect of oxyphencyclimine-hydroxyzine on gastric acid. *American Journal of Gastroenterology*, 1962, 38, 460-469.

The effect on gastric acidity of the combination oxyphencyclimine-hydroxyzine was examined in a group of 50 patients, using multiple intragastric electrodes to follow focal gastric pH in 25, and aspiration and titration of gastric contents in the other 25. Typical diagnoses were: duodenal ulcer, benign gastric ulcer, etc. The usual choice was 10 mg oxyphencyclimine and 25 mg hydroxyzine; onset of action varied from 18 to 120 minutes with a duration of 1-4 hours. Oxyphencyclimine was somewhat effective as an anticholinergic and its action was potentiated by its combination with hydroxyzine. Twenty-five of the patients were evaluated clinically and the combination found effective in relieving symptoms of gastrointestinal origin, regardless of the fact that the mechanism of such symptoms is not understood.

Section of Gastroenterology
Department of Medicine
Hahnemann Medical College and Hospital
Philadelphia, Pa.

2013 Berthier, Ch. J., Bouvard, J., & Viret, G. A propos de deux psychoses puerpérales. Evolution clinique et thérapeutique. Intérêt des courbes d'excitabilité neuromusculaire. [On 2 cases of puerperal psychoses. Clinical and therapeutic course. The importance of the neuromuscular excitability curves.] *Lyon Médical*, 1962, No. 1008, 647-648. [Abstract]

Two cases of postpartum psychosis are described. One woman responded to neuroleptics [unspecified], perfusion and cortisone; the other, after the failure of the neuroleptics, recovered after 1 series of insulin shock therapy. Repeated studies of these patients using excitability curves guided proper therapy and confirmed the

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validity of the concepts of Laborit, Coirault, et al.

[No address]

2014 Stucki, D., & Gross, J. Etude clinique du "Librium" au cours de l'accouchement. [Clinical study of Librium used at delivery.] Praxis, 1962, No. 24, 624-633.

One-hundred women were given 50 mg i.m. injections of chlordiazepoxide (Librium), sometimes repeated, at childbirth. Fifty-five were primiparas. In 17 cases chlordiazepoxide was used with morphine, while in the remaining 83 it was used alone. Behavior was much improved in 40 and improved in 15. Control of pain was excellent in 25 instances and average in 15. Chlordiazepoxide is useful in obstetrics because of its psychorelaxant, myorelaxant and analgesic properties.

Hôpital de district de Porrentruy
Service de gynécologie et d'obstétrique
Porrentruy, Switzerland

2015 Bhaskaran, K., & Nand, D. Satya. Prochlorperazine in chronic schizophrenia. Journal of the Indian Medical Association, 1962, 39, 91-93.

Prochlorperazine (25 mg t.i.d. p.o. for 1 week, then 50 mg t.i.d. for 3 weeks, continued if necessary as maintenance therapy) was administered to 45 chronic schizophrenics (31 unclassified, 9 paranoid and 5 catatonic) aged 20-44 years (mean duration of illness 4.2 years) for 22-60 days. Routine laboratory tests were performed. Clinical response was assessed by 2 investigators. Of the 45 patients, 14 recovered, 3 improved markedly, 15 improved, 12 were unchanged and 1 was withdrawn from the study due to development of severe extrapyramidal symptoms. Comparatively severe extrapyramidal symptoms occurred in 3 other patients, but concurrent administration of promethazine effectively controlled these reactions. No other side effects were encountered. Overall, 32% of the patients recovered, 41% improved and 27% failed to improve.

Hospital for Mental Diseases
Ranchi, India

2016 Schreier, Arthur J., Reznikoff, Marvin, & Glueck, Bernard C. Controlled clinical evaluation of acute schizophrenia: a comparative study of rating instruments and judges. Comprehensive Psychiatry, 1962, 3, 343-353.

Twenty-seven hospitalized patients, participating in a drug evaluation project [details not stated], were utilized to compare the effectiveness of 6 different rating scales designed to describe clinical change in an acute schizophrenic population during a 6-week period. Raters included physicians, nurses and aides. The following scales were used: Global M.D., Institute of Living Scale-Physicians Form (IOL, M.D.), Q-sort, Global Nurses, Institute of Living Scale-Nursing Personnel Form (IOL, Nurses) and Burdock Ward Behavior Inventory. The results were discussed at length and interpreted as indicating the need for considerable improvement in methods of rating. The highest inter-rater reliability occurred in the doctor's Global Judgement based on the 1 hour interview. Lack of agreement among the 3 nursing scales was 29%, but the 3 physicians' scales indicated a 61% order of consistency.

Institute of Living
Hartford, Conn.

2017 Pincherle, M., & Morgante, R. Trattamento delle sindromi depressive con fenelzina (Nardil). [Treatment of depressive syndrome with phenelzine (Nardil).] Archivio di Psicologia, Neurologia e Psichiatria, 1962, 23, 45-49.

Thirty subjects, most ambulatory, were treated with phenelzine (usually 15 mg t.i.d., but in 2 cases used i.v.). Nine cases of endogenous depression, 13 reactive depression and 8 involutional depression were included. Remissions were obtained in 63.33%, partial remission in 13.33% and negative results in 23.4%. Side effects were negligible. Slight hypotension appeared in 7 patients, controlled by dosage reduction.

Cattedra di Semeiotica Medica
Università di Bologna
Bologna, Italy

2018 Paquay, J., Arnould, F., Burton, P., Massart, C., Chantraine, J., Meurice, E., & Pairoux. Etude clinique d'un nouveau neuroleptique: le Sordinol. [Clinical trial of a new neuroleptic: Sordinol.] *Annales Médico-Psychologiques*, 1962, 120, 1, 314.

Sordinol, a derivative of chlorprothixene, was used for 11 months in 92 patients of various categories. The average dose was 120-150 mg/day, though in some cases 225 mg/day for several months. The drug was efficacious with an action comparable to that of haloperidol. It was generally well-supported with negligible side effects but should only be used with prudence, especially for major states of agitation. In 3 cases of confusional agitation in epileptics Sordinol gave excellent results.

[No address]

2019 Lopez-Ibor, J. The "target" symptoms in the treatment of depressions. *Comprehensive Psychiatry*, 1962, 3, 15-19.

Criteria in the diagnoses of reactive and endogenous depressions are discussed. Also, situational sadness is contrasted with vital sadness (Freud's Trauer und Melancholie), and the latter symptom is considered bound to endogenous depression. In a group of 125 patients diagnosed as depressives without specifying the type, successful therapy was reported for 51.2%; however if only the group with vital depression is considered, then the remission rate jumps to 84.48%. Of the 12 cases unresponsive to chemotherapy, 7 were responsive to ECT alone or combined with imipramine. Imipramine is not a euphoric drug, but acts as a muffler. The action is analogous to the effect of chlorpromazine in the treatment of schizophrenia. The delusions disappear because the disorder of the depth of the mood from which they emerge is toned down. For diagnostic purposes, a modified Funkenstein's test for the prediction of imipramine tolerance was developed. A full minute was used for the

i.v. injection of 50 mg acetylcholine; blood pressure levels were determined before and after 3, 5, 8, 10 and 20 minutes. Imipramine was better tolerated by patients with sympatheticotonic or fast vagotonic responses. A major drop in arterial pressure without recovery at the final reading, characteristic for marked vagotonus, indicates a poor tolerance for imipramine.

[No address]

2020 van Leeuwen, D.P., & Scholl, F.S.K. Promazine hydrochloride (Prazine) tijdens de baring. [Promazine hydrochloride (Prazine) during delivery.] *Geneeskundige Gids*, 1962, 40, 161-164.

A mixture of promazine and pethidine (25 mg of each i.m., i.v. or both) was used during labor in 32 obstetric patients, including 20 primiparas. Analgesic and sedative effects were excellent, especially by the i.v. route, and there were no side effects in either the mother or the infant. The use of promazine significantly reduced the total amount of opiates and other narcotics required during labor. Figures for forceps deliveries and total duration of labor were within normal limits.

Gynaecologische-Verloskundige afdeeling
Gemeenteziekenhuizen te Gravenhage
Hague, The Netherlands

2021 Hanna, Calvin, Mazuzan, John E., Jr., & Abajian, John, Jr. An evaluation of dihydromorphine in treating post-operative pain. *Anesthesia and Analgesia*, 1962, 41, 755-760.

Following major surgical procedures expected to produce moderate to severe pain, 76 patients, aged 21 to 67 years, in a double-blind study comparing the pain-relieving action of dihydromorphine to morphine, meperidine and alphaprodine (all drugs in mg/70 kg i.m.), received dihydromorphine (1-4 mg), morphine (7-10 mg), meperidine (75-100 mg) or alphaprodine (40 mg) with levallorphan (0.8 mg). Of the 76 patients, 39 received a 2nd injection in a crossover study. Drugs used in the crossover (mg/70 kg

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i.m.), received dihydromorphinone (1-4 mg), morphine (7-10 mg), meperidine (75-100 mg) or alphaprodine (40 mg) with levallorphan (0.8 mg). Of the 76 patients, 39 received a 2nd injection in a crossover study. Drugs used in the crossover (mg/70 kg i.m.) were: dihydromorphinone (1-2 mg), morphine (7-10 mg) and meperidine (75-100 mg). Within 3 hours, 10 mg of morphine was equivalent to ca. 1.5 mg of dihydromorphinone (ratio 1:7) with respect to onset, maximal activity and length of drug action. Meperidine at 75 mg or alphaprodine at 40 mg manifested similar onset of action and time of maximal activity but a decrease in duration of effect. Nausea and vomiting were not troublesome side effects with dihydromorphinone. Dihydromorphinone has several advantages over the newer narcotics, but additional evaluations are strongly recommended.

Department of Pharmacology
University of Arkansas Medical Center
Little Rock, Ark.

2022 Geissmann, P., & Sichel, C. A propos d'un nouveau cas d'hallucinoſe visuo-verbale chez un nŕvrosŕ obsessionnel. Rŕsultats favorables du traitement par l'imipramine. [On a new case of visual-verbal hallucinosis in an obsessional neurotic. Favorable results with imipramine treatment.] *Annales Mŕdico-Psychologiques*, 1962, 120, 1, 403-404.

A second case of visual-verbal hallucinosis, analogous to that first reported by Kammerer, Israel and Geissmann (1959), in a 27-year-old man, is reported. He suffered from repeated depressive episodes with hallucinations. Treatment with high doses [unspecified] of imipramine suppressed hallucinations and depressive phases so that the subject could undergo psychotherapy.

[No address]

2023 Dunlop, Edwin. Inhibition of enzymic activity by intravenous drug therapy. *Acta Neurologica Scandinavica*, 1962, 38, 71-72.

Over 100 patients with diversified depressive conditions, who failed to respond to

current therapy and were in acute need of treatment, received nialamide 1 mg/ml administered by i.v. drip for 3 hours. The initial 500 mg/day dosage had been increased to 1000 mg/day by 250 mg/day increments. Blood pressure was monitored on a Winston Blood Pressure Follower. Results indicated that i.v. administration of MAO inhibitors was superior to oral medication at regular dosage levels, and amelioration thus achieved was equivalent to that produced by any current antidepressant therapy. Corroboration of the findings was reflected in EEG changes, autonomic responses and the level of urinary tryptamine excretion. Other compounds tested similarly include etryptamine, amitryptiline, imipramine, phenelzine and the demethyl analogues of amitryptiline and imipramine. Nialamide was most efficacious due to its relative lack of toxicity.

Fuller Memorial Sanatorium
South Attleboro, Mass.

2024 Blumenfeld, Margaret, Suntay, Remedios G., & Harmel, Merel H. Sodium gamma-hydroxybutyric acid: a new anesthetic adjuvant. *Anesthesia and Analgesia*, 1962, 41, 721-726.

The properties of the sodium salt of α -hydroxybutyric acid are reviewed and outlined. This drug was administered to 26 surgical patients, aged 7 months to 82 years, in doses ranging from 0.65 gm to 8.0 gm. Surgery included thoracic, abdominal and orthopedic procedures as well as neurosurgical operations. Patients selected for this trial were generally classified as poor risks. For these patients in particular the following advantages were noted with this drug: it produced relaxation of the jaw muscles and permitted extensive manipulation of the upper airway and epiglottis without spasm or "bucking." The drug did not depress spontaneous ventilation but facilitated the use of controlled ventilation while exerting no circulatory depressant action. Its use with nitrous oxide markedly reduced the need for other analgesic agents during anesthesia. The major drawback of sodium α -hydroxybutyric acid is its lengthy induction period, with 30 minutes the shortest recorded anesthetic time to operation. This

slow onset and long duration (2 to 3 hours) of action indicates its advantage in the longer surgical procedures. Although this small series of patients does not warrant any general conclusions, it does confirm the positive claims made for this drug.

Department of Anesthesiology
State University of New York
Downstate Medical Center
Brooklyn, N. Y.

2025 Carter, Charles H. Antiemetic specificity of carphenazine in brain damage. A blind crossover study with acetophenazine. *American Journal of Gastroenterology*, 1962, 38, 587-591.

Carphenazine (18.75-150 mg/day) and acetophenazine (30-120 mg/day) were tested for the control of vomiting in a crossover study of 49 brain-damaged subjects, ranging in age from 6 months to 38 years. Most were children, aged 6 to 16 years; the mean age for the group was 12 years of age. Carphenazine had proven extremely effective in a previous study as an antiemetic agent in these patients, completely controlling severe and persistent vomiting and rumination in 102 out of 110, and was virtually lifesaving in several instances. When carphenazine was withdrawn, 29 of the 49 patients who had not vomited on this agent, resumed serious vomiting. Acetophenazine was then given to these 29, and 15 experienced a 75-100% control of the symptom while 14 were controlled 50% or less. Carphenazine was reinstituted for these 14 and achieved complete control in 13 cases. No troublesome side effects of any kind appeared with either of these agents at the dosage levels used.

Sunland Training Center
Orlando, Fla.

2026 Kelley, J. Whitney. Management of psychiatric disorders with diazepam. *Clinical Medicine*, 1962, 69, 1789-1802.

One-hundred-and-nine depressed outpatients, aged 16-89 years, with various psychiatric and neuropsychiatric disorders (involuntary psychosis, schizophrenia, con-

version reaction, depressive reaction with anxiety, CBS, etc.), average duration of disease 2.7 years, received diazepam (5-10 mg t.i.d., with slight variations) as an adjunct to intensive psychotherapy given for an average of 14 weeks. In addition to diazepam, 2 patients received progesterone, 1 chlordiazepoxide and 5 ECT. A very satisfactory response was obtained in 66 patients, a moderate response in 24 and an unsatisfactory response in 18. Considerable improvement was shown, with diminution of tension, increased optimism and renewed interest in everyday events. Patients became more amenable to psychotherapy. Many elderly patients experienced significant improvement in mood, with resultant augmentation of insight. Side effects occurred in 33 patients (lassitude, ataxia, dizziness, gastrointestinal distress, etc.) and necessitated discontinuance of therapy in 9. Diazepam was by far the most effective chemotherapeutic agent for psychomotor depression, and involutional and postinvolutional psychotic reactions. It is less effective than chlordiazepoxide as an anxiolytic agent except in patients with concomitant depressive symptoms.

[No address]

2027 Royer, P., Poire, R., Rayel L., & Trouvenot, P. Action du Daranide dans l'épilepsie. Premiers essais cliniques. [The action of Daranide in epilepsy. Initial clinical trials.] *Annales Médico-Psychologiques*, 1962, 120, 1, 402.

Daranide [no details], in addition to the barbiturates, has a particularly favorable effect on the classic components of psychic epilepsy, having a tranquilizing action on ideomotor processes.

[No address]

2028 Bobon, J., Collard, J., & Demaret, A. L'imipramine (Tofranil) à faibles doses en gériatrie mentale. [Imipramine (Tofranil) at low doses in psychiatric geriatrics.] *Annales Médico-Psychologiques*, 1962, 120, 1, 424.

Imipramine (10-40 mg/day) was adminis-

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tered to elderly mental patients. Global therapeutic results were variable. The 2 symptoms most influenced were depression, and social and locomotor inertia. In some cases the side effect excitation necessitated interruption of treatment. Imipramine has a decidedly favorable effect in a significant minority of cases.

[No address]

2029 Singer, L., Geissmann, P., Depoutot, J. C., & Gutbub, Th. Resultats thérapeutiques du MD 2028 M.D. [Therapeutic results with MD 2028.] *Annales Médico-Psychologiques*, 1962, 120, 1, 402.

Sixty-three cases of agitation were treated with MD 2028 [dosage unspecified]. The agent had excellent psychiatric activity, allowing a better therapeutic approach, especially in relation to the suppression of psychomotor excitation. MD 2028 potentiates phenothiazine derivatives. Side effects include parkinsonism, and cardiovascular and respiratory reactions. The latter reactions necessitate strict medical surveillance. MD 2028 should not be used in combination with phenothiazine derivatives.

[No address]

2030 Schlemm, Walter. Erfahrungen mit einem neuen Phenothiazin-Derivat in der Gynäkologie und Geburtshilfe. [Results with a new phenothiazine derivative in gynecology and obstetrics.] *Medizinische Monatsschrift* 1962, 16, 33-34.

Six-hundred hospitalized female patients received triflupromazine in doses of 10-20 mg i.m. The drug was very effectively used in post-operative patients (vomiting was controlled in 89.8%), and in patients with hyperemesis gravidarum (vomiting was controlled in 78.7%). It also proved to be a very efficient tranquilizing agent in cases of excessive agitation due to emotional factors and cerebral sclerosis. In these cases 1 injection (20 mg i.m.) was administered, followed by 10 mg p.o. t.i.d. Triflupromazine was very effective during delivery when 10 mg i.m. was given during cervical dilatation. Triflupromazine reduces the

need for analgesics and sedatives during delivery and has no untoward effects on mother or newborn. No cardiovascular or allergic side effects were observed.

Klinik Dr. Geisenhofer
Trivolistrasse
Munich, Germany

2031 Luminet, M.D., & de Dowiakowski M.L. Etude clinique d'un nouveau thymoleptique: le Parnate SKF. [Clinical study of a new thymoleptic: Parnate SKF.] *Annales Médico-Psychologiques*, 1962, 120, 1, 315.

Six unslected cases of depression were studied with tranlycypromine [(Parnate) dosage unspecified]. Food, appetite, sleep and activity were assessed. The latter aspect was most influenced. Sometimes tranquilizers were combined in the treatment. Tranlycypromine appeared particularly effective in the control of hypochondria. An improvement of 60% was noted.

[No address]

2032 Rossier, M. Essais d'un nouveau tensiolytique psychique en médecine générale: le "Control-OM." [Trial of a new psychotensiolytic in general medicine: Control-OM.] *Praxis*, 1962, 11, 291-293.

Eighty patients with subjective states involving anxiety, nervous-tension, obsession, etc. were treated with mephenoalone (Control-OM; e.g., 0.5g t.i.d. or q.i.d.). Forty cured or markedly improved and 20 improved cases were obtained. Treatment was interrupted in 8 cases because of toxicity: 1 allergic reaction (urticaria), 1 agitation and 6 cases of cramps. Extrapyramidal reactions were also noted and some hypotension, as well as constipation, diarrhea, hypersomnia, fatigue and diminution of libido.

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Lausanne, Switzerland

2033 Walker, Robert B. Clinical experience with anticholinergic-tranquilizer in gastrointestinal disorders. *Clinical Medi-*

cine, 1962, 69, 859-870.

A series of 42 patients, aged 20-60 years, with anxiety and stress secondary to psychogenic or organic disease of the gastrointestinal tract, sometimes complicated by heart disease or hypertension, received capsules containing 5 mg chlördiazepoxide and 2.5 mg quazran bromide p.o. q.i.d. for 1 to 7 days to several weeks. A great improvement or complete disappearance of symptoms occurred in 24 patients, partial remission was observed in 13, and some improvement in 2. Most patients (88%) were asymptomatic in 2-7 days. Treatment was a failure in only 3 instances, due to heartburn and excessive fatigue, which constituted the only side effects aside from single instances of constipation and difficulty in micturition. The combined drug enabled several patients to obviate the possibility of relapse into their pattern of chronicity. During periods of stress, many patients found it advantageous to take capsules at their own discretion.

No address]

2034 Kramer, John C., Klein, Donald F., & Fink, Max. Imipramine as an adjunct to phenothiazine therapy. *Comprehensive Psychiatry*, 1962, 3, 377-380.

Of 58 patients receiving imipramine and a phenothiazine derivative 32 patients (29 schizophrenics, 2 depressed and 1 psychoneurotic), aged 17-60 years, received chlorpromazine (minimal daily dose 300 mg; modal dose 1200 mg) or prochlorperazine (minimal and modal dose 60 mg) for 4 weeks, and imipramine (minimal daily dose 25 mg; modal dose 300 mg) was added for at least an additional 3 weeks. The mean period of combined treatment was 11 weeks. All patients received sufficient procyclidine to obviate any drug-induced parkinsonian symptoms. In addition, 9 patients were treated initially with imipramine (dosages same as above) followed by chlorpromazine or prochlorperazine, and 17 patients had other patterns of treatment. Of the 32 patients, 22 were improved, 6 were unchanged and 4 were made worse. Favorable increases were observed in motor activity and verbal expression. Those who manifested

the greatest diminution of lethargy, boredom and withdrawal were least likely to have an increase of overt anger and hostility. Side effects in 10 of the 32 cases included involuntary body movements characterized by stammering, difficulty in swallowing and involuntary twitching of the mouth and face, suggestive of myoclonic seizures. Reduction in drug dosage resulted in amelioration. The 4 young, bizarrely ruminative schizophrenic males, who were worse after imipramine was added to the regimen, became subjectively happier but more overtly psychotic with combined drug therapy.

Department of Experimental Psychiatry
Hillside Hospital
Glen Oaks, L. I., N. Y.

2035 Hsu, B., & Kin, K. C. Pharmacological study of tetrahydropalmatine and its analogs. A new type of central depressants. *Archives internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 318-327.

A series of animal experiments and trials on hospital patients were designed to test the effects of tetrahydropalmatine (THP) and its analogues since 1955. In studies of THP analgesic effects and sedative-tranquilizing action, rabbits, hospital patients, mice, cats and monkeys were used in tests which included: prolongation of hexobarbital sleeping time, influence on spontaneous motor activity, action on amphetamine toxicity, influence on mescaline action, influence on avoidance conditioning, behavioral influence (in monkeys) and influence on cerebral electrical activity (in rabbits). Results indicate that THP, which has marked analgesic, sedative and hypnotic activity, may be a new type of CNS depressant. Its levorotatory isomer exerts inhibitory effects, while the dextrorotatory isomer does not, and sometimes even provokes transient excitation. THP exerts considerable effects on the cerebral cortex and subcortical structures. The main site of its action is probably located in the subcortical areas. Among the THP analogues, Corydalis L (which contains the aporphine nucleus) has marked analgesic potency with weak sedative and hypnotic activity, while the tetrahydroberberine exerts a stronger sedative-tranquilizing action with a slight analgesic effect. Study of

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the structure-activity relationships indicates that the integrity of the mother nucleus of THP and the saturation of the 3rd ring are essential for central depressant action. For tetrahydroberberine the methylenedioxy group is 1 of the active groups. A working hypothesis is proposed for further synthesis of new tranquilizing drugs.

Institute of Materia Medica
Academia Sinica
Shanghai, China

2036 Vidal, M. G., Vidal, B., & Valery, M. B. Essais cliniques de la trimépropimine (7162 RP). [Clinical trials with trimépropimine (RP 7162)]. *Annales Médico-Psychologiques*, 1962, 120, 1, 422.

Trimépropimine (300 mg/day) was used in the treatment of 50 cases [depression]. Global improvement was 15 remissions, 13 markedly improved, 14 slightly improved and 8 were failures. Two patients suffered an epileptic fit during therapy. The antidepressive, sedative and anxiolytic actions of trimépropimine make this drug a valuable antidepressant.

[No address]

2037 Kramer, John C. Single daily dose schedules of imipramine (Tofranil). *Comprehensive Psychiatry*, 1962, 3, 191-192.

Imipramine (75-300 mg/day, mean dosage 150 mg/day) was administered in a single daily dose (SDD) or as a multiple daily dose (MDD) to 14 voluntary hospitalized patients, aged 17-60 years, for 1-5 months. Behavioral alterations observed with SDD and MDD regimens included decreased depression, decreased apathy and withdrawal, diminished preoccupation with somatic symptoms or obsessions and increased activity. In 6 patients who received imipramine initially on a SDD basis, therapeutic response varied from minimal to good. Of 8 patients placed on the SDD regimen after previous MDD therapy, 4 showed additional behavioral improvement and 3 maintained the behavioral changes initiated during the MDD period. On SDD, 1 patient became increasingly hostile towards a new physician although

she remained seclusive and passively cooperative in the ward setting. Deleterious effects with SDD included dizziness, headache, sweating, nausea, dry mouth, blurred vision and hypnagogic hallucinations. No appreciable change occurred in severity or frequency of these undesirable effects in patients changed from MDD to SDD aside from 2 exceptions in which hypnagogic hallucinations and nausea occurred in 1, and dizziness in another. The tendency toward slow onset of action and absence of rapid fluctuation in mood and behavior of patients on SDD suggests that slow pharmacological action may be a critical characteristic of these psychotropic drugs, and that blood levels of these drugs may not be reflective of drug action at the cellular level.

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2038 Janke, Horst. Zur Objektivierung der Wirkung der Meprobamatkombination Sedapon. [Objective determination of the effect of the meprobamate combination Sedapon. *Münchener Medizinische Wochenschrift*, 1962, 104, 277-280.

A group of 50 randomly selected patients with vegetative syndromes related to the viscera (functional disturbances of heart circulation and climacteric complaints) received Sedapon (150 mg meprobamate, 2 mg yohimbine and 0.13 mg pure belladonna alkaloid per tablet), 2-4 tablets daily for 1 day to 4 weeks. Of these, 35 experienced symptomatic relief and 10 showed some degree of improvement. Young people responded better than older persons. Sedapon proved less effective as adjunctive therapy in the follow-up treatment of cardiovascular disease. In order to avoid errors due to subjective judgment, a double-blind study was conducted with 80 other patients. Those receiving the drug showed excellent improvement in 26 instances, and satisfactory improvement in 7. Placebos produced improvement in only 5 cases. No side effects were noted.

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Oldenburg, Germany

2039 Martin, P., & Goffaux, P. Evaluation clinique des propriétés psychotropes de l'amitriptyline. [Clinical evaluation of amitriptyline's psychotropic properties.] *Annales Médico-Psychologiques*, 1962, 120, 1, 313-314.

Ninety-six patients, 76 of whom were cyclothymic, were given evening doses [unspecified] of amitriptyline. These patients had previously been treated with imipramine without good results. Amitriptyline provided superior therapy. The drug is, at the same time, both a sedative and anxiolytic.

[No address]

2040 Hardy, T. K., & Wakely, D. The amnesic properties of hyoscine and atropine in pre-anaesthetic medication. *Anaesthesia*, 1962, 17, 331-336.

In a double-blind study, the amnesic properties of atropine and hyoscine, in customary preanesthetic doses, were compared in 200 patients undergoing minor surgery. Half were given 0.6 mg atropine and the rest 0.4 mg hyoscine s.c. Morphine was conventionally administered as preoperative sedation. Immediately before anesthesia each patient was shown a single-line drawing of one of 5 common objects, namely a cat, an umbrella, etc. and asked to identify it. Six to 12 hours after the operation the patient was visited and if he volunteered any information about the pictures he was directly asked if he remembered seeing a picture. In the hyoscine group 7 had no memory of the picture shown them, while all of the atropine patients had recall. A total of 87% receiving hyoscine had no memory impairment. Although hyoscine was found to possess amnesic properties greater than those of atropine, results failed to justify its reputation as an amnesic agent.

Department of Anesthetics
Royal Infirmary
Cardiff, Great Britain

2041 Findlay, Charles W., Jr. The value of promethazine hydrochloride in preparing patients for peroral endoscopy. *American Review of Respiratory Diseases*, 1962, 86, 272-274.

Promethazine was given as premedication for endoscopy in 100 patients, the majority of whom were bronchoscope. Promethazine was given i.m. 90 minutes before endoscopy; 65% of the patients were given 50 mg, and the remaining 35% received 25 mg. Additionally, 15 patients received 100 mg promethazine on the night before endoscopy; there was a tendency to give very anxious subjects heavier premedication. Other drugs used at conventional dosages were meperidine, morphine, codeine, scopolamine and atropine. Suitable relaxation and appropriate responses were obtained from 80% of the patients. Maximal drying effect was obtained from 80% of the patients. Maximal drying effect was obtained from promethazine in conjunction with either atropine or scopolamine, while the combination of promethazine with meperidine lessened apprehension. Promethazine materially aided in predicting patient response.

Francis Delafield Hospital
New York, N. Y.

2042 Hussen, Jan-Hinnerk, & Scholz, Werner. Psychopharmakotherapie mit Librium in der Tuberculose-Behandlung. [Psychotherapeutic use of Librium (chlordiazepoxide) in the treatment of tuberculosis.] *Medizinische Monatsschrift*, 1962, 16, 176-178.

Fifty-six tubercular patients, 8 of whom were female, from 25 to 29 years of age, were treated with 10 mg chlordiazepoxide usually t.i.d. with some variation. Psychically labile patients and those who were troubled, querulous, or agitated or suffering from anxiety, depression or insomnia, were treated with satisfactory to excellent results in 52 cases, and without success in 4 cases. These 4 patients were extremely ill, suffering also from considerable reduction of the breathing surface and dyspnea, and in 3 of these cases side effects were noted, consisting of vomiting (1), increased depression (1) and general malaise (1). Otherwise no side effects were noted.

Städtisches Waldkrankenhaus
Berlin-Frohnau, Germany

2043 Hashkes, Henry R. Evaluation and

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pattern response of a benzquinamide in 50 patients. *Clinical Medicine*, 1962, 69, 2239-2244

Fifty patients, aged 14-80 years, with acute, subacute, chronic or reactivated anxiety and tension, nausea and vomiting or muscular spasms received benzquinamide (25 mg p.o., q.i.d.) for an average of 2 weeks. Some patients with severe nausea, cardiac neurosis and palpitation received 50 mg t.i.d. or q.i.d., p.o. Initial response to the average dose fluctuated from a few hours to a few days, while those receiving the 50 mg dose schedule frequently responded within 1 hour. Of the 36 acute reactions, 23 had excellent responses, 8 good, 1 fair and 4 poor. Psychiatric referral was necessary for 2 individuals (schizoid and involuntional reactions). Benzquinamide provided varying degrees of effective relief from anxiety (27 excellent, 10 good, 1 fair and 2 poor responses) and nausea (5 excellent and 1 good response) in the majority of patients, with an excellent or good response achieved by 86%. The drug was not valuable in alleviating muscle spasms (1 fair and 3 poor responses). No untoward side effects occurred in any of the patients. Concurrent therapy in 5 cases with an analgesic, vasodilator, or anticholinergic resulted in marked potentiation of drug effects.

[No address]

2044 Bram, G. Treatment of psychoneurotic conditions with long acting trifluoperazine (Stelazine), spansule capsules. *British Journal of Clinical Practice*, 1962, 16, 143-145.

Trifluoperazine sustained release capsules (supplemented when necessary by 1 mg tablets) were administered p.o. b.i.d. or t.i.d. for 2 months to 114 psychoneurotic patients suffering from tension, restlessness and panicky attacks. Individual adjustments in dosage produced marked improvement or complete relief from symptoms in 39 patients, marked improvement in 56, slight improvement in 6 and no demonstrable change in 13. Patients with endogenous depression and agitation failed to respond uniformly to the drug. No significant side effects were observed. Illustrative case histories of 4 patients, aged 34-62 years, are presented.

[No address]

2045 Cameron, D. Ewen, Lohrenz, J. G., & Handcock, K.A. The depatterning treatment of schizophrenia. *Comprehensive Psychiatry*, 1962, 3, 65-76.

Thirty schizophrenics, aged 20-61 years treated during short-term hospitalization in general hospitals received ECT, continuous sleep (patients were awaked 3 times daily for meals and toilet) and barbitol, secobarbital, phenobarbital, chlorpromazine or RO4-1038 (serine-N²-isopropylhydrazide) [dosages unspecified]. Complete recovery occurred in 1 case, 19 were improved and 9 showed social recovery. Amnesia was common. Patients were followed for a mean of 35.2 months, during which maintenance ECT was administered as required.

Allan Memorial Institute
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Canada

2046 Tosetti, K., & Schlegel, Ch. Die Wirkung der Phenothiazine auf den Foeten und das Neugeborene. [The effect of phenothiazines on the fetus and newborn.] *Zeitschrift für Ärztliche Fortbildung*, 1962, 20, 112-114.

The effect of chlorpromazine was investigated (A) on the fetus, (B) during delivery and (C) on the newborn. One-hundred-and-twenty cases in the 8th month of 1st pregnancy were investigated (A). The single dose of chlorpromazine was 50 mg i.m. Twenty minutes after administration, registration of the fetal heart beat was carried out by means of an electrophonocardiograph. The frequency of heartbeats was investigated (B) in 50 cases, at the time when the cervical orifice was dilated 4-5 cm and labor pains were strong and regular. The observations were carried out over a period of 45 minutes to 3 hours. The results in (A) and (B) were within the range of L₁ and regarded as physiological. Of 2481 deliveries, no complications were noted (C) in 93.06% of babies whose mothers had not received chlorpromazine; 91.99% of babies whose mothers had received it showed no significant influence on the breathing

enter or frequency of aspirations. In a 2nd series, chlorpromazine (25 mg) combined with pethidine (100 mg) was administered to 100 patients under the same conditions and results compared with 2101 normal deliveries. Spontaneous breathing rate was reduced to 91% and if delivery occurred 3-6 hours after the injection, the rate was reduced to 83.8%. The administration of phenothiazines does not damage the fetus or newborn significantly; the cumulative effects of certain combinations, however, are to be warned against.

No address]

2047 Carsley, S.H., & Olson, John A. Use of fluphenazine dihydrochloride for relief of anxiety. *Clinical Medicine*, 1962, 69, 717-720.

Of 277 patients given fluphenazine (0.25 mg tablet b.i.d. and/or 1 gm sustained-release capsule once daily) for anxiety relief in a variety of organic and functional disorders (e.g., menopausal syndrome and spastic colitis), 222 obtained notable symptomatic relief. Patients suffering from phobias and anxiety associated with gastrointestinal disturbances, as well as neurodermatitis cases, got best results. Success was obtained in patients with anxiety derived from personal problems; 30% of the highly excited patients were treated with barbiturates to help them sleep or provide daytime sedation. Side effects included "bizarre feelings", an increase of prior tremors and drowsiness.

No address]

2048 Alexander, Howard G. Electroconvulsive and nonconvulsive stimulation combined with trifluoperazine in treating schizophrenic patients. *Journal of Neuropsychiatry*, 1962, 3, 388-389.

A group of 323 female schizophrenics, age 18-42 years, received trifluoperazine (5 mg b.i.d., then 5 mg/day for maintenance) in combination with ECT twice daily for 5-6 days, after which nonconvulsive stimulation was administered alternately for 8 more treatments. After 3 weeks, 75% were free of psychotic symptoms. Of 109 1st admissions (82%) left the hospital within 90 days after

admission, their average hospital stay being 48 days. Of 145 readmissions, 93 (64%) were in remission and out of the hospital within 90 days. Of 62 patients returned from furlough with relatives, 30 (43%) were in remission and on furlough again within 90 days of their return. The proper ratio of convulsive and non-convulsive electrical stimulation in combination with trifluoperazine offers the fastest and most efficient means of relieving the psychotic symptoms in schizophrenia.

Wichita Falls State Hospital
Lake Wichita, Tex.

2049 Maletz, Leo. Use of a neuroleptic-antidepressant combination in office practice. *Journal of Neuropsychiatry*, 1962, 4, 35-38.

A combination tablet containing trifluoperazine (1 mg) and tranlylcypromine (10 mg) was administered t.i.d. to 54 psychiatric patients, aged 23-72 years, most of whom had acute depressive reactions accompanied by mild to moderate anxiety, for 1-9 months. Dynamic psychotherapy was performed concomitantly. Close supervision minimized the danger of suicide. Criteria for improvement included overall symptomatic relief, ability to participate in psychotherapy, degree of insight attained and changes in capacity to function socially and vocationally. Results revealed that 24 patients (44%) were much improved, 18 (34%) were improved, and 12 (22%) remained unchanged or unimproved. Symptomatic improvement usually occurred within 5 days of treatment. Restoration of concupiscence heralded rapid overall improvement. During the course of the evaluation, treatment was discontinued in 11 patients who had experienced initial improvement, and treatment with other tranquilizers or antidepressants was substituted. While 3 continued to improve, 8 experienced a return of their symptoms within 1 week. Symptoms were again alleviated by the drug combination. Side effects occurred in 12 patients and included insomnia, headache, constipation, dizziness and restlessness.

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Clinical studies
Abstracts 2050-2052

2050 Roper, Peter, Effect of multiple-shock electroconvulsive therapy on a paranoid delusional system. *Journal of Neuropsychiatry*, 1962, 4, 28-30.

A 42-year-old man with a highly systematized paranoid delusional system received chlorpromazine (50 mg q.i.d.) and 9 ECT treatments within 12 days, after which he was less agitated. More intensive ECT was instituted on a daily basis for 4 consecutive days, whereupon the patient's delusional system disappeared completely. After 9 intensive ECT sessions, a program of 3 regular ECT treatments per week was re-instituted. A total of 22 ECT treatments (9 Page-Russell intensive treatments) were administered over 1 month, and the patient recovered sufficiently to be discharged from the hospital 6 weeks after admission.

Allan Memorial Institute
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Canada

2051 Papadopoulos, C. N., & Keats, Arthur S. Specific and nonspecific antagonism of morphine-induced respiratory depression. *Anesthesiology*, 1962, 23, 86-91.

To compare the efficacy of nalorphine to that of methylphenidate against a therapeutic dose of morphine, 6 healthy men, aged 22-27 years, received morphine (10 mg/day) for 4 days in tests at intervals of 4-25 days. Placebo, 7 mg nalorphine and 10-30 mg methylphenidate were administered i.v. in randomized order. As well, 3 subjects were given 30 mg methylphenidate i.v. without morphine in a separate study and effects were measured 1 and 3 hours later. Morphine effects were measured 60-90 minutes following drug administration and antagonist effects were determined 120-150 minutes after morphine administration. Measurement of respiratory depression was made in terms of the displacement of each subject's alveolar CO₂ tension-alveolar ventilation curve produced by the drug when compared to a control curve which was previously obtained. Alveolar air was continuously sampled and passed through an infrared CO₂ analyzer. Subjective effects were estimated by questioning

the subjects. In antagonizing morphine-induced respiratory depression, 30 mg methylphenidate was as effective as 30 mg nalorphine. Methylphenidate antagonism was associated with no change in oxygen uptake and persisting sedation. As methylphenidate was as effective as nalorphine and more effective in antagonizing psychomotor depression, it is best to treat various degrees of depression as well as excessive depression from therapeutic doses of narcotics with a nonspecific antagonist although the increased oxygen uptake on methylphenidate may not be advantageous.

Division of Anesthesiology
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Houston, Tex.

2052 Coirault, R., Jarret, T., Ramel, P., Cadour, E., Croco, L., & Vincent, J. Dimethyl-amino-ethyl ester of para-chlorophenoxy acetic acid -- its psychopathological action. *Journal of Neuropsychiatry*, 1962, 3, 367-374.

Centrophenoxine (300-600 mg/day p.o. 250 mg i.v. in 10 cc serum) was administered for 16 months to 230 patients with deficiency states, confusional states, psychosis, neurosis, autonomic nervous system disturbances and endocrine disorders. In 8 illustrative case histories of deficiency states, centrophenoxine exerted the following modifying effects: behavior improved and re-socialization was facilitated, intellectual functions increased in efficacy, spatial orientation was augmented, speech disturbances diminished or disappeared (depending upon the severity of the neurological lesion) and mood was stabilized. Centrophenoxine therapy was optimal in 10 cases with confusional states, when regrouping of intellectual and thymic processes permitted improved adaptation to reality. With 10 cases of endogenous melancholia, centrophenoxine alone was ineffectual and frequently aggravated anxiety. Combination of centrophenoxine with imipramine, nialamide or prochlorpromazine was efficacious in such cases. Centrophenoxine was contraindicated in 24 patients with delirium or schizophrenia, as it markedly aggravated

these conditions. Excellent results have been observed in patients with hysteria. Corroboration of clinical observations was obtained in 20 patients evaluated by means of Benton's Visual Retention Test, the MMPI and the Wechsler Bellevue Chart of IQ and Deterioration Test. Centrophenoxine increases objectivization and intellectualization, producing a tranquilizing and relaxing effect that is beneficial in numerous anxiety states. In borderline cases, the drug acts as a revelator, permitting more rapid and accurate diagnosis. The drug's mechanism of action centers in the cortical and thalamo-cortical areas, while regulating various functions of the hypothalamic-hypophyseal region.

Clinique Neuropsychiatrique
Saint-de-Grâce
Paris, France

2053 Kurland, Albert A., & Gruenwald, Frances. Clinical experiences with 1,3,3 tricyano-2-amino propene (U-9189) in chronically ill psychotic patients. *Journal of Neuropsychiatry*, 1962, 3, 393-398.

Sixteen chronic female psychotics, aged 17-52 years, (13 schizophrenic, 2 mentally defective and 1 psychotic with organic brain disease) received 1,3,3 tricyano-2-amino propene (U-9189), 200-250 mg/day for 1 week, 400-500 mg/day for the 2nd week, 600-750 mg/day for the 3rd week and 800 mg/day for 3 more weeks. Patients were seen daily by the psychiatrist, and routine hematology and urinalysis was performed weekly. Only 1 patient exhibited a positive response to the treatment procedure. Minimal changes occurred in 6 patients and 9 showed increasing excitation. Complications included gastrointestinal disturbances (vomiting) and dermatological reactions. Five case histories of patients previously treated with phenothiazine tranquilizers are included. Other experimental work revealed that U-9189 increased the protein content in neuronal cells. Residual effects of phenothiazines may have influenced the results of the above study.

Research Department
Spring Grove State Hospital
Baltimore 28, Md.

2054 Monnerot, E., Chabert, G., & Barre, R. L'éventail thérapeutique: un correcteur des neuroleptiques, le R. 381-382 (Califon). [Clinical note: an antineuroleptic, R 381-382 (Califon).] *Annales Médico-Psychologiques*, 1962, 120, 1, 419.

Eighteen cases of drug-induced extrapyramidal reaction were treated with phenmetrazine [(Califon; R 381-382) dosage unspecified]. The drug was capable of suppressing neuroleptic side effects and inhibited weight gain caused by neuroleptics. No side effects occurred with phenmetrazine.

[No address]

2055 Dornette, William H. L., Poe, Mary F., Cavallaro, Richard J., & Sheffield, William E. A double-blind study of Tacaryl as a narcotic potentiator when used for preliminary medication. *Anesthesia and Analgesia*, 1962, 41, 32-36.

In a double-blind study methdilazine (Tacaryl) was used as a narcotic potentiator in 4 groups comprising 195 patients awaiting surgery. This drug is classified as an antihistaminic. One hour before anesthesia, in addition to 0.43 mg atropine i.m., the following schedules were followed: 31 patients received placebo (0.5 cc), 55 50 mg pethidine and 12.5 mg methdilazine, 51 100 mg pethidine and placebo, and 58 12.5 mg methdilazine. No clearcut differences were noted in any of the 3 drug groups, but the combination gave a higher influence of respiratory minute volume depression than either drug used alone. Methdilazine potentiated pethidine so that the pethidine dosage could be reduced by half.

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2056 Ekbohm, K. A. Treatment of migraine, Horton's syndrome and restless legs with Deseril (UML-491). *Acta Neurologica Scandinavica*, 1962, 38, 313-318.

Methysergide (UML-491; 4-6 mg/day p.o.) was administered to 64 patients (42 with migraine, 4 with Horton's syndrome, 5 with

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chronic headache and 16 with restless legs) for several months to over a year. Side effects, predominantly nausea and vomiting, occurred in 25 patients, and were severe enough to necessitate drug discontinuation in 14 patients. Migraine headaches were ameliorated in 26 patients. In Horton's syndrome, some improvement was noted but too few patients were treated to permit definite conclusions. Methysergide produced no improvement in chronic headache. While 8 patients with restless legs showed improvement, earlier studies in which placebos caused improvement in this syndrome cast doubt on the validity of the improvement observed.

Akademiska Sjukhuset
Uppsala, Sweden

2057 Wright, Stanley W., Valente, Mario, & Tarjan, George. Medical problems on a ward of a hospital for the mentally retarded. *American Journal of Diseases of Children*, 1962, 104, 111-113.

This report, intended as an aid for physicians in counseling parents before and after institutionalization of the young, severely mentally retarded child, gives a general description of the daily activities, medical care and common illnesses of 76 children, most from 2 to 10 years of age, hospitalized in the Pacific State Hospital. Chlorpromazine, prochlorperazine, trifluoperazine, meprobamate and promazine [no dosage schedules] are efficacious in controlling serious behavior problems in these children; phenobarbital, often with diphenylhydantoin, is used in the control of seizures. Facilities, personnel, and budgets are briefly reviewed. Information which should be supplied to parents is cited. Pediatricians should assume a leadership role in the improvement of such institutional programs.

Research Department
Pacific State Hospital
Pomona, Calif.

2058 Wrede, J. Erfahrungen mit Marsilid bei Depressionen. [Results with Marsilid in depressions.] *Der Nervenarzt*, 1962, 33, 30-32.

Eighty-two patients were treated with iproniazid (Marsilid): 59 hospitalized patients (50-100 mg t.i.d.) for 6-8 weeks, and 23 ambulatory patients (25 mg 3-8 times p.d.) for up to 2 weeks. Of the hospitalized patients 16 were suffering from endogenous depression, 6 were manic-depressives, 4 were treated for climacteric depressions, and 13 had involutional depressions. Three patients were treated for depressions with paranoid overtones and 3 for depressions with hypochondria. Excellent improvement was obtained in 9 patients, good in 6 and fair to insignificant in 11. No effect was noted in 18 patients. There were 2 suicides, and 13 dropouts due to side effects or lack of cooperation. Of the ambulatory patients 6 were treated successfully. In 17 other patients no definite results could be ascertained. Of 53 patients who were followed throughout, 21% showed excellent results; 15% responded well and 30% showed fair or temporary improvement. No effect was noted in 28% and a negative effect in 6%.

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Rottweil, Germany

2059 Cox, E. M., Holmes, J. W., & Lougheed, J. C. A study of trimethobenzamide, an antiemetic, in surgical patients. *Clinical Medicine*, 1962, 69, 2205-2213.

Trimethobenzamide (100 mg p.o. every 4 hours for 6 doses) was administered to 75 patients on admission (22 surgical and 53 nonsurgical patients with a history of nausea and vomiting and 40 without) to determine side effects. In addition, 97 surgical patients, aged 16-85 years, received trimethobenzamide postoperatively (100-400 mg p.o. or i.m. every 4 hours for 6 or more doses for 2-11 days), administered prophylactically in 49 and for nausea and vomiting in 48. Change in degree of nausea and vomiting before and after drug administration was evaluated on a 0-3 point rating scale. Of the 49 patients who received the drug as a postoperative prophylactic, 35 had no nausea or vomiting. Of the 70 surgical patients with nausea and vomiting, 32 had an excellent response to therapy, 21 had good responses, 11 fair and 6 poor. Therapy was effective in 64 patients (91%). Some corre-

tion was observed between site of surgical procedure and degree of nausea and vomiting. Side effects involved only 1 case of minimal drowsiness and dizziness. Triethobenzamide is especially useful in older patients in whom depression is undesirable.

No address]

2060 Brandt, A. L., Lui, S. C. Y., & Briggs, Bernard D. Trial of chlordiazepoxide as a preanesthetic medication. *Anesthesia and analgesia*, 1962, 41, 556-557.

In the 1st part of a 2-part double-blind trial of preanesthetic medications, 48 patients received 25-50 mg chlordiazepoxide, 25 received 100 mg pentobarbital and 25 received placebo; in the 2nd portion, 49 patients received 50 mg chlordiazepoxide, 25 received 100 mg pentobarbital and 50 received placebo, all drugs administered as capsule the night before surgery and 1 capsule 2 hours before surgery. Blood pressure and pulse rates were recorded at various intervals. Drug efficacy was evaluated by the anesthesiologist, ward personnel and patients. Results evaluated by the Kolmogorov-Smirnov 1-tailed, 2-sample test were found to be statistically significant. The combined result was also statistically significant. In the combined studies, 71.6% had a satisfactory night's sleep with chlordiazepoxide, as did 77% with pentobarbital and 44% with placebo. Comparable effects were produced by 50 mg chlordiazepoxide and 100 mg pentobarbital and both provided highly satisfactory psychosedation, while 25 mg chlordiazepoxide and placebo were ineffective. For sound and sufficient sleep on the night preceding surgery, pentobarbital and 50 mg chlordiazepoxide were both effective while 25 mg chlordiazepoxide was ineffective. In reducing anxiety, 25 mg chlordiazepoxide was as effective as 50 mg. No side effects were noted. Chlordiazepoxide was found to be an effective preanesthetic agent without the disadvantages commonly associated with other ataractic drugs.

San Francisco State University School of Medicine
San Francisco, Calif.

2061 Plotz, Milton. Oxanamide in anxiety and tension states. *Clinical Medicine*, 1962, 69, 708-712.

In a single-blind 10 week study, 39 office patients suffering mild anxiety and tension were treated with either a vitamin fortified 400 mg oxanamide capsule, given q.i.d., or a vitamin capsule alone on alternate weeks. Most patients ultimately refused the vitamin capsule due to ineffectiveness in comparison to the drug. Improvement was noted in 70% on the drug, while there was no real response to the vitamins alone. Drug response was best in mild neurosis and poorest in those with more serious difficulties. Side effects, most occurring within the 1st 2 weeks of the study, included gastrointestinal upset and drowsiness. Oxanamide administration on alternate days is adequate for many patients with temporary or minor emotional disturbances. Its use in agita pectoris should be further investigated.

Brooklyn State Hospital
Brooklyn, N. Y.

2062 Hüter, K. A. Vergleichende Untersuchungen zur psychoprophylaktischen und medikamentösen Geburtsleitung unter besonderer Berücksichtigung der Neugeborenenasphyxie [Comparative investigations on the "psychoprophylactic" and drug-supported delivery, with special consideration of the asphyxia of the newborn.] *Geburtshilfe und Frauenheilkunde*, 1962, 3, 279-289.

Four-hundred-and thirty-six women were thoroughly prepared for natural childbirth. The aim was to shorten the duration of delivery, ease labor pains, avoid complications, keep the mother aware of the childbirth and avoid possible harm to the breathing center of the newborn. For evaluation, the women were grouped in 4 groups. 85.6%, groups I and II, were regarded as complete success. In group I the duration of delivery was normal, little pain was felt, the patient was quiet and disciplined and no medication was needed. Group II differed only in one respect: antispasmodic medication or pethidine was administered. Groups III and IV, a total of 14.4%, were regarded as "failures". The patients were restless, complained of

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severe labor pains and demanded medication. They received a lytic mixture, consisting of 50 mg chlorpromazine, 100 mg pethidine and 50 mg promethazine. The deliveries in these last 2 groups took twice as long as in Groups I and II. The quota of asphyxia of the babies, and therefore the danger of physical and mental damage to the baby, is directly proportional to the duration of the delivery, concerning frequency of incident as well as severeness.

Frauenklinik der Medizinischen Akademie
Düsseldorf, Germany

2063 Ramquist, Nils, & Jonsson, Carl-Otto. Insulin-glykosterabi vid schizofreni. [Insulin-glucose therapy in schizophrenia.] *Nordisk Medicin*, 1962, 67, 371-375.

The milder therapeutic effects of insulin-glucose therapy were compared to standard insulin coma therapy at conventional dosages in 109 schizophrenic females. In order to make the 2 groups of patients comparable they were matched according to the type of schizophrenic reaction, length of illness and age, etc. No serious side effects were seen with insulin-glucose therapy but some cases showed gastrointestinal symptoms resulting from heavy glucose intake. No definitive rate of improvement was stated because the standard, insulin coma therapy, has not been conclusively shown superior to placebo or barbiturate induced sleep. In cases where insulin coma therapy is considered, insulin-glucose therapy is advocated because it offers less risk.

Beckomberga Sjukhus
Bromma, Sweden

2064 Itil, T. Die Problematik der Schlafstörungen und deren Beeinflussung. [Problems of disturbances of sleep and their treatment.] *Arzneimittel Forschung*, 1962, 12, 399-407.

EEG methods were used to determine the effects on duration and depth of sleep of 11 patients following i.v. administration of a combination drug Itridal, (40 mg prothipendyl and 150 mg cyclobarbitol in 2 ml Homburg-Solution B). The effects of the

combination were compared with the effects of each drug singly, at the same and double the dosage, and the potentiating effects of the drugs, both singly and in combination upon thiopental were also determined, for another 4 patients. All 15 persons were free from motor unrest, and the EEG's showed no abnormalities when taken with the patients at rest. EEG tracings for Itridal show the effects of each of the two components (alpha-activation, reduced amplitude and frequencies) but Itridal-induced sleep is longer and deeper than that obtained with double the dosage of either drug singly. Both the individual components and the combination potentiate thiopental. Further clinical comparisons for 23 healthy persons indicate a clearcut superiority of either component over the placebo, and of Itridal over either component. In tests on 100 patients with sleep disturbances of varying origin Itridal proved effective in improving sleep and was judged as better than barbiturates in combating sleep disturbances of psychomotor origin.

Neuro-psychiatrisches Universitäts-Klinik
Erlangen-Nürnberg, Germany

2065 Jost, F., & Weber, E. Kurz- und Langzeitbehandlungen der depressiven Syndrome mit "Laroxyl" (Amitriptylin). [Short and long-term treatment of depressive syndromes with Laroxyl (amitriptyline).] *Praxis*, 1962, 51, 650-656.

Sixty-two depressive patients were treated of whom 32 had endogenous depression, psychogenic depression, 9 depressive schizophrenia and 7 with reactive depression suffering from arteriosclerosis, debility and psychopathic states. Treatment duration was less than 1 month to more than 24 months with an average duration of 28 days. Dosages of amitriptyline averaged 150-200 mg per day, i.m. or orally at maintenance doses after discharge were 50 mg per day. Side effects were slight, the most frequent being dry mouth, constipation, slurred speech, excessive perspiration, with occasional dizziness, tremors, tachycardia, subfebrile reaction, headaches, orthostasis and weariness. Seven of the 62 were completely cured, 39 showed improvement, and 16 showed no change.

Three relapses were reported in the moderate improvement-group. Amitriptyline potentiates the effect of imipramine, chlorazepoxide and chlorprothixene. Caution must be observed when used with MAO inhibitors. A suicide attempt with the drug is reported, where, after therapy, the patient was discharged and placed on an ambulatory schedule of amitriptyline.

Heilanstalt Beverin
Grazis, Graubünden
Switzerland

2066 Thalmann, R. Depressionsbehandlung mit einem neuen Antidepressivum "Laroxyl" (Roche). [Treatment of depression with a new antidepressant Laroxyl (amitriptyline).] Praxis, 1962, 51, 671-676.

Sixty-eight patients, varying in age from 20 to 80 years, were treated with varying doses of amitriptyline up to a maximum of 100 mg per day for a 6-month period. The patients fell into 3 categories: endogenous depression, reactive depression and chronically depressed schizophrenics. Newly admitted patients were mostly treated by injections, all others being treated with tablets. Good to very good results were obtained in 41 cases. The highest percentage of poor results was registered with depressed schizophrenics. Laboratory tests on blood and liver function yielded no significant changes; blood pressure and pulse were not affected. Side effects were slight; dry mouth, slight vertigo and somnolence, and mild tremors in the fingers. Maintenance doses after discharge were 50-100 mg/day.

Heil- und Pflegeanstalt Münsingen
Münsingen, Switzerland

2067 Bauer, R., & Matthée, K. Klinische Erfahrungen bei der Kombination eines Perphenazins mit einem neuartigen zentralen Stimulans. [Clinical experiences with the combination of a perphenazine derivative and a new CNS stimulant.] Medizinische Monatsschrift, 1962, 16, 328-331.

Twenty-three patients, 60 schizophrenic, were treated with 1 of the 3 varieties of the new combination drug MF 11a, b, or d,

consisting of 10 mg thiopropazate and 30, 15 and 25 mg respectively of KSW 788 (a bicyclic central stimulant). MF 11a and b are tablets, and 11d is in ampoule form. Doses varied from 3-8 tablets daily, and in acute psychoses to as much as 12 tablets daily. Ampoules were used parenterally only when tablets could not be administered. MF 11b was used at the end of the treatment period, which lasted 2-4 months. Tolerance was good. Side effects included psychomotor unrest, esophageal spasms, and parkinsonism, the latter being noted in patients who had similarly reacted to other drugs including perphenazine. MF 11 was administered with fair to excellent results to 40 patients, and with no effect or poor results in 33. The drug is effective in rigid, catatonic or hebephrenic schizophrenics, as well as in the majority of chronic schizophrenics.

Heil- und Pflegeanstalt
Lohr am Main, Germany

2068 Archer, Joel S., Smessaert, Andre A., & Hicks, Robert G. Phenothiazine tranquilizers in anesthesia. Review with report on fluphenazine. New York State Journal of Medicine, 1962, 62, 828-833.

In a double-blind study on over 200 women, aged 20-45 years, scheduled for dilatation and curettage, fluphenazine or placebo was administered postoperatively. A 5% incidence of retching and vomiting occurred with fluphenazine and a 14% incidence with placebo. With fluphenazine, recovery was more serene; there were no noticeable differences in blood pressure and pulse. Although hypotension and tachycardia are possible complications, judicious use of the newer phenothiazine derivatives with the piperazine nucleus poses no threat.

Department of Anesthesiology
St. Vincent's Hospital
New York, N. Y.

2069 Carpenter, Frederick A., Steinhaus, John E., Webb, Sam C., & Thompson, Raleigh. Evaluation of preanesthetic medication. Anesthesiology, 1962, 23, 141-142.

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Skin resistance and the psychogalvanic reflex (PGR) were used as criteria in a double-blind study of apprehension following administration of surgical preanesthetic agents (all on a weight basis, 3.0 ml/150 pounds i.m.). Immediately before surgery, 50 patients (10 in each group), 15-60 years of age, received pentobarbital (90 mg/150 pounds), meperidine (75 mg/150 pounds), promethazine (37.5 mg/150 pounds), hydroxyzine (150 mg/150 pounds) or placebo. A 15-minute control period before drug administration was used to determine changes in skin resistance caused by the PGR (stimulated by standardized light flashes.). Drug administration was followed by a test period of 1 hour divided into 4 15-minute periods during which the light flash occurred 3 times at random intervals. The resultant skin resistance changes were read directly from the recorder. Although the group slope of meperidine showed considerable difference from placebo, a scattergraph of meperidine indicated wide variability in individual response. Promethazine's group slope differed least from placebo, but a scattergraph showed consistent action. Differences between the scores of each drug and placebo were highly significant. To test correlation of rating scales and the PGR, an additional study was undertaken with 5 patients using the same drugs and placebo at 3 dose levels. Each patient was simultaneously evaluated by PGR changes and 7-point rating scales by 2 independent observers. The correlation was highly significant at the 0.5% level of confidence. The PGR may merely mirror changes in peripheral autonomic reactions due to the drugs tested. Further studies will attempt to demonstrate dose effect.

Department of Anesthesiology
Grady Memorial Hospital
Atlanta, Ga.

2070 Haase, H. -J. Intensität und Äquivalenz neuroleptischer Wirkung und ihre therapeutische Bedeutung. [Effectiveness and equivalence of psycholeptic agents and their therapeutic importance.] *Nervenarzt*, 1962, 33, 213-220.

Psycholeptic drugs act mainly on the extrapyramidal tracts which effect psychomotor

activity, tensions and psychotic sensations. Fifty selected patients with comparable symptoms (43 schizophrenics, 3 manics and 3 atypical psychotics) divided in five groups of 10 each received daily p.o. doses of 200-450 mg chlorpromazine, 50-90 mg prochlorperazine, 10-20 mg of trifluoperazine, 4-12 mg fluphenazine and 4-10 mg thiopropazine. Patients were treated for 15 days and effects for the 1st days and for each subsequent 5-day period were considered. The following parameters were evaluated: clinical symptoms, hyperactivity, somnolence, dyskinetic reaction and coarse tremor. More than 1900 figures were presented in tabular form. Symptoms were equally ameliorated by all drugs. Thiopropazine produced severe extrapyramidal symptoms, possibly caused by overdosages. Hypermotility was effectively reduced by all drugs. Somnolence was most prevalent with chlorpromazine. Severe hyperkinetic reactions occurred approximately twice as often with fluphenazine and thiopropazine as with chlorpromazine. A slight degree of coarse akinesia developed with all drugs, frequently in combination with minor rigor.

Psychiatrische Klinik der Medizinischen
Akademia
Düsseldorf, Germany

2071 Gschlacht, V.E. Die ambulante Behandlung depressiver Zustände mit Laroxyl (Roche). [Treatment of ambulatory depressive states with Laroxyl (Roche).] *Praxis*, 1962, 51, 657-660.

Thirty-five patients, including 12 psycho-reactive depressives, 15 endogenous depressives, and 8 involutional depressives, were treated with initial doses of 10 mg amitriptyline (Laroxyl) t.i.d. After 1 week doses were increased as required to 25 mg tablets t.i.d. or more, the maximal daily dosage being 150 mg. Maintenance doses were 1-2 10 mg tablets daily. Duration of treatment varied 1-6 months. Tolerance was excellent, mild vertigo or tremor of the fingers, sweating or dry mouth being noted in a few cases. Only 5 patients did not respond to the drug; 8 improved, and 22 were cured. All involutional depressives were cured. Amitriptyline's effects fa

into 2 components: an early trophotropic-neuroleptic reaction and a subsequent ergotropic-thymoleptic component.

[No address]

2072 Anton, A. Ergebnisse einer klinischen Prüfung des Neuroleptikums Ciatyl. [Clinical trials with the neuroleptic drug Ciatyl.] *Medizinische Welt*, 1962, 12, 665-669.

The chlorperphenthixene derivative Ciatyl is available in tablets of 10 mg and 25 mg, and in 1 ml ampoules (2.5% solution). The drug was administered parenterally and orally to 115 patients, mostly males, with psychoses or organic brain disorders, at doses of 50 mg t.i.d. at the start, down to as little as 1-25 mg tablet per day. Somnolence occurs in the earlier periods, as well as weight increases of 2-3 kg, possibly due to a lowering of the BMR. Some mild slowing down of reaction times will occur which stops when the drug is withdrawn. Even schizophrenics who suffer from fears of poisoning appear willing to take the drug, and admit to subjective feelings of sedation and freedom from anxiety or fear. Ciatyl is effective in combating unrest and aggression in senile dementia, trauma and arteriosclerosis of the brain, brain atrophy and chorea major. Side effects are unimportant; they include parkinsonian symptoms, dry mouth, heart palpitations, tendency to collapse, oppressive sensations in the head and heart; on the other hand, there are some positive side effects, such as suppression of colic in gall- and kidney stone cases, and suppression of smooth-muscle spasms. Alcohol intolerance may result in ambulatory treatment. Ciatyl acts on the reticular formation, thalamus, hypothalamus and nucleus ruber, and has a true antipsychotic effect.

Westfallischer Landeskrankenhaus
Münster, Germany

2073 Paley, Herbert M., Hankoff, Leon D., Kawi, Ali A., & Mendelsohn, Frederick S. The therapeutic profile of haloperidol. A preliminary study of a butyrophenone derivative in in-patients and out-patients.

Journal of Neuropsychiatry, 1962, 4, 39-42.

A 4-point Target Symptom Rating Scale (TSRS) was employed to evaluate several different dimensions of clinical change in 29 schizophrenics (in- and outpatients), aged 19-57 years, who received haloperidol (1-5 mg t.i.d.) for 3 days to 3 months (mean duration for inpatients, 11.2 days), and 7 inpatient schizophrenics, aged 26-49 years, who received chlorpromazine (100 mg t.i.d. or q.i.d., average daily dose 370 mg) for a mean duration of 10.5 days. Improvement with haloperidol was significant in relation to manifest anxiety, paranoid symptoms and hallucinations; with chlorpromazine, statistically significant improvement was found in manifest anxiety, paranoid symptoms and structural thought disorder, etc. Agitation and apathy also improved. Haloperidol was therapeutically comparable to chlorpromazine. Extrapyramidal side effects of haloperidol were observed in 22 of the 29 patients: 9 had severe, principally akinetic Parkinsonian manifestations and 5 displayed acute episodes of dystonic movements. Therapy was discontinued in 3 outpatients and 1 inpatient. No gastrointestinal side effects occurred, but moderate hypotension was observed in 10 out of 17 patients. Drowsiness was reported by 5 patients. The therapeutic profile of haloperidol as examined by means of the TSRS appeared to approximate that of chlorpromazine. Haloperidol did not exert an analeptic effect on apathy and depression in the schizophrenic patients under study.

Department of Psychiatry
Downstate Medical Center,
State University of New York
606 Winthrop Street
Brooklyn 3, N.Y.

2074 Lorenz, K., & Schmidt, G. Klinische und elektroenzephalographische Beobachtungen bei und nach Chorea minor. [Clinical and electroencephalographic observations during and after chorea minor.] *Deutsche Gesundheitswesen*, 1962, 17, 35, 1499-1506.

Sixty-two chorea minor patients, 3-20 years old (some with a medical history of somatic or psychic disturbances before onset of

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chorea) were treated conventionally. Sleep therapy was uniformly effective in 6 severe cases. Use of Fowler's solution frequently resulted in changes in the blood picture, the most frequent being leukocytopenia and, particularly granulocytopenia. Trihexyphenidyl seems to be beneficial. Endo- and myocarditis was observed in 44 patients (73%). Post-discharge examinations of 40 patients showed cardiac involvements in only 43%. Recidivism was high in comparison with other rheumatic conditions. Behavioral or physical disturbances were found in 31 of 43 discharged patients one year later, but onset of puberty was frequently a concomitant factor. However, 50% of the cases were damaged psychically or intellectually.

Kinderklinik
Medizinische Akademie
Dresden, Germany

2075 Horstmann, W. Erfahrungen mit einem barbituratreien Schlaf- und Beruhigungsmittel bei jungen Kindern. Klinische und elektroenzephalographische Untersuchungen mit 2,4-Dioxo-3,3-diäthyl-5-methylpiperidin (Noludar). [Experiences with a barbiturate-free hypnotic and sedative for small children. Clinical and electroencephalographic study with 2,4-dioxo-3,3-diethyl-5-methyl-piperidine (Noludar).] Münchener Medizinische Wochenschrift, 1962, 104, 603-608.

Methypylon (Noludar) was used with a large number of clinical visits over a 5-year period, supplemented by records of 260 examinations performed on 226 children. It has proven useful as a sedative and hypnotic of medium duration with a wide range of clinical indications, including sedation of newborn with birth trauma, preparation for examinations (e.g., EEG'S, ECG'S). Only side effects noted are nausea and vomiting shortly after administration of the drug. No toxic effects have been noted with respect to hematopoiesis, renal and hepatic function, respiration, circulation, etc. Tolerance is good, so that dosages while perhaps requiring adjustment to individual needs, can be varied widely. Mean dosages are recommended by age groups, averaging ca. 30-35 mg/kg.

Universitäts-Kinderklinik Freiburg
Freiburg, Germany

2076 Gennerich, E. Prüfung eines neuer barbiturfreen Hypnotikums Toquilone in der Psychiatrischen Klinik. [Trial of the new barbiturate-free hypnotic drug Toquilone in a psychiatric clinic.] Praxis, 1962, 13, 340-343.

Twenty-six patients (18 schizophrenics, 8 others) were treated with hypnotics for a total of 982 nights, 50% of the observations being for Toquilone, and the remaining 50% being distributed among a number of other drugs, both barbiturates and barbiturate-free compounds. Good to excellent results were obtained for the 8 nonschizophrenics and for 13 of the 18 schizophrenics. The remaining 5 retrogressed under Toquilone treatment. In only 1 patient, with spasmolytic effects, were any unfavorable side effects noted. The action of the drug may best be compared to that of some of the barbiturate-free sedatives, but it is also moderately comparable to barbiturates. It is particularly indicated for nonschizophrenics with moderate sleep disturbances, but it is also useful in combination with 50-100 mg chlorpromazine in the treatment of schizophrenics.

Psychiatrische Klinik Hasenbühl
Liestal, Switzerland

2077 Kivalo, E., & Amnell, G. Die Behandlung von Oligophrenen mit Librium unter besonderer Berücksichtigung der Gehirnläsionen. [The treatment of oligophrenia with Librium with some considerations on brain lesions.] Psychiatrie, Neurologie und Medizinische Psychologie, 1962, 144, 176-183.

Forty-one oligophrenic patients (9 psychomotor agitation, 13 spasticity, 13 choreo-athetosis and 11 with other indications and 5 patients presenting more than 1 symptom) were treated with chlordiazepoxide (Librium) for an average of 4 months. Dosage was 5-10 mg b.i.d. In 4 out of 9 patients with psychomotor agitation response was satisfactory. About 3/4 of the spastics and choreo-athetosis patients re-

ponded well to therapy. In 5 cases psychomotor agitation occurred which necessitated the interruption of treatment. Drowsiness, which occurred in 4 other cases, disappeared upon dosage reduction. No anti-convulsant effect was apparent at the dosages used. Chlordiazepoxide is of value in the treatment of oligophrenics, and its value increases with the level of the patient's mental development.

Centralanstalt Rinnekoti
Helsinki, Finland

2078 Fiume, Sebastiano. Sperimentazione clinica di un nuovo preparato ad azione antidepressiva. [Clinical experimentation with a new antidepressant.] Clinica Terapeutica, 1962, 22, 339-344.

Twenty-five cases of depression were treated with amitriptyline; the average daily dose was 100 mg (50-150 mg) p.o. or i.m. Global results were 18 remissions, 1 clearly improved and 6 cases slightly improved. Of 9 cases with a previous history of depression, 8 were cured and 1 improved slightly. Of 10 new cases of depression, 7 were cured, 1 improved and 2 improved slightly. In the 6 cases of involutional depression with concomitant cardiovascular complications, 3 were cured, while the other 3 improved slightly. Generally, improvement was rapid, occurring in the first few days of treatment. Side effects were virtually absent.

La Lago di Lesina, 53
Rome, Italy

2079 Mendes, J. Fragoso, & Da Silva, Lopes. Tratamento psicofarmacológico da ansiedade pela metaminodiazepoxide. [Psychopharmacologic treatment of anxiety with chlordiazepoxide (methaminodiazepoxide).] Journal do Medico (Porto), 1962, 47, 117-125.

Two-hundred-and-thirty-six patients with various anxiety states were treated with chlordiazepoxide. The daily dosage of chlordiazepoxide was 20-75 mg, and 10 mg/day was used as a maintenance dose; the duration of treatment was 3-8 weeks. Global

results were: 62 remissions, 101 satisfactory, 33 fair and 40 negative. A pilot double-blind crossover study was made with 8 patients; results for chlordiazepoxide versus placebo were: improvement-4:1; aggravation of the condition followed by some improvement-0:1; initial improvement followed by slight worsening-2:2; no alteration-2:3, and progressive worsening-0:1. The results of the double-blind study did not warrant definite conclusions. The only prominent side effect from chlordiazepoxide was daytime drowsiness.

Clinica Psiquiátrica da Faculdade de
Medicina de Lisboa
Lisbon, Portugal

2080 Katz, Robert A., Aldes, John H., & Rector, Mina. A new drug approach to muscle relaxation. Journal of Neuropsychiatry, 1962, 3, Suppl. 1, S91-S95.

Diazepam (25-40 mg/day p.o., parenteral for 3-5 days in acute patients, then p.o.) was administered to 84 patients, aged 20-77 years, with musculoskeletal disorders arising from trauma, neurological orthopedic and arthritic diseases for an average of 4 weeks. Outstanding symptoms were muscle spasm and pain. Marked improvement in 57 patients included diminished spasticity, alleviation of pain and increased motion. A moderate response occurred in 15, with adequate but not remarkable improvement in spasticity and pain, along with increased ambulation. A minimal response was obtained by 4, and 4 failed to respond. Drowsiness occurred with high doses of diazepam in elderly patients. There were no indications of toxic reactions or habituation, and laboratory data remained negative and within normal range. Final evaluation was withheld in 4 patients. Diazepam has a definite place in the management of musculoskeletal disorders associated with emotional overtones.

Ben R. Meyer Rehabilitation Center
Cedars of Lebanon Hospital
Los Angeles, Calif.

2081 Vilkin, M.I., & Lomas, J.B. Clinical

Clinical studies
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experience with diazepam in general psychiatric practice. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S139-S144.

Diazepam (5 mg t.i.d. or q.i.d.) was administered to 83 patients (42 with anxiety reactions, 23 severe agitated depression, 12 schizophrenic reactions and 6 chronic alcoholics with anxiety), aged 14-78 years, for more than 6 months. Improvement was evaluated by the patient, his family and physician. Several patients who manifested immediate improvement received placebos and experienced a return of symptoms within a few days. Excellent results occurred in 28 patients, good in 20, fair in 21 and negative in 14. The most gratifying results were obtained in anxiety reactions. Mild to moderate depressions with agitation responded well, moderately depressed and agitated patients responded to diazepam and imipramine [dosage unspecified]. Severely depressed patients required ECT. Diazepam ameliorated anxiety in alcoholics. The phenothiazines, especially trifluoperazine, are preferable in treating acute schizophrenia. Side effects from diazepam included dizziness and decreased coordination when performing athletic endeavors.

Westwood Hospital
Los Angeles, Calif.

2082 Collard, J. Clinical experience with diazepam in neurosis. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S157-S158.

Diazepam (15 mg/day) was administered to 25 neurotics (psychoneurotic depression, anxiety, compulsion or conversion neurosis, etc.) with anxiety, psychic tension, depression and psychosomatic symptoms for 1-8 weeks. Symptoms and results were assessed on a 0-4 point rating scale. Positive results were obtained in 68% of the patients. Diazepam is a good anxiolytic in moderate and mild cases of neurotic non-melancholic anxiety. The drug also produces symptomatic relief of psychic tension of moderate intensity, but lacks the characteristics of a true antidepressant. Sleep was normalized in 12 out of 13 cases. Excellent inhibition of algebras, spasms and psychosomatic tachycardia was also observed. In addition, mean anxiolytic activity indices

were calculated for diazepam, chlordiazepoxide, meprobamate and placebo.

Hoffmann-LaRoche Inc.
Nutley, N.J.

2083 Ruesch, Jurgen. The treatment of acute psychoses. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S122-S129.

A comprehensive treatise on the management of acute psychoses includes a discussion on the 4 major approaches to psychiatric treatment, the classic theories of psychosis and the modern concept of acute psychosis as an unspecific reaction, evaluation of treatment programs, the role of social therapy, drug and psychotherapy in the overall treatment plan and results of the treatment of acute psychoses. The Acute Treatment Service of the Langley Porter Neuropsychiatric Institute has treated 263 patients from December 1960 to February 1962, 100 of whom had acute psychoses. The mean age of these patients was 39 years. Diagnostically, 12 had depressive reactions, 54 were schizophrenic, 21 had involutional psychoses, 9 schizo-affective reactions and 4 acute situational disturbances. Of the 100, 88 received the psychoactive drug [dosages and therapeutic results unspecified]: 71 received phenothiazines, 12 received antianxiety drugs (chlordiazepoxide and meprobamate) and 25 received psychomotor energizers (tranlycypromine and imipramine). The average hospital stay was 41 days, but no extensive followup work has been pursued.

University of California School of Medicine
The Langley Porter Neuropsychiatric
Institute
San Francisco, Calif.

2084 Proctor, Richard C. The improved management of incapacitating anxiety states. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S151-S154.

Diazepam (5-10 mg t.i.d. or q.i.d.) was administered to 51 patients aged 25-58 years with anxiety, often accompanied by depression, insomnia, nervousness and restlessness, for an average of 11 weeks.

Routine laboratory tests were performed before and after the study. Results were evaluated according to degree of relief of symptomatology reported by patients and observed in psychiatric interviews. Although patients failed to return for follow-up studies, 6 manifested excellent responses, 28 had good responses and 16 had poor responses. Diazepam was particularly effective in alleviating anxiety, which in turn brought prompt improvement in the remaining symptoms. Patients also experienced an increased ability to adjust to stressful situations. Of 12 patients with anxiety and depression, 1 patient had an excellent response and 6 had good responses. Side effects occurring in 9 patients included sedation, nausea, dizziness, constipation and a sensation of light-headedness or silliness. Drug discontinuation was also mandatory in 4 patients due to severity of side effects.

Department of Psychiatry
Bowman Gray School of Medicine
Wake Forest College
Winston-Salem, N.C.

2085 Merlis, Sidney, Turner, William J., & Krumholz, Wilhelm. A double-blind comparison of diazepam, chlordiazepoxide, and chlorpromazine in psychotic patients. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, 33-138.

In a single-blind study, 80 chronic patients, aged 14-62 years (32 schizophrenics, 5 psychotics with psychopathic personality), divided into 4 groups, received a lactose placebo, chlorpromazine (50 mg), diazepam (10 mg) or chlordiazepoxide (25 mg), all administered as 1 capsule t.i.d. for 4 weeks. The 2 rating scales used for weekly evaluation were the brief psychiatric rating scale (BPRS) and the modified Malamud-Sands Scale (MMS). No significant evidence was found to suggest that 1 agent was superior to the others. Analysis of the BPRS scores by the Kruskal-Wallis nor parametric analysis of variance revealed that diazepam was most effective in 2 wards, while the remaining 2 wards indicated that chlordiazepoxide and chlorpromazine gave the best results. Overall, 19 patients showed clinical improvement in some area of

psychopathology, but 4 on diazepam deteriorated. Of those who improved, 6 received placebo, 6 chlorpromazine, 3 diazepam and 4 chlordiazepoxide.

Research Division
Central Islip State Hospital
Central Islip, N. Y.

2086 Borenstein, P., Dabbah, M., & Blès, G. Etude électroencéphalographique de l'halopéridol. [Electroencephalographic study of haloperidol.] *Annales Medico-psychologiques*, 1962, 120, 1, 133-141.

Haloperidol 5 mg was administered i.p. once only to 32 patients (7 epileptics, 7 schizophrenics, 8 with behavioral problems, 10 miscellaneous) and EEG's taken 45-60 minutes later. Improvement, more stable alpha waves, was noted in 16, 3 retrogressed and 13 remained unchanged. Anomalies were noted in 7 cases, consisting of degraded points and pointwaves, and modifications of the theta and delta components where these had been present. Another 40 patients (15 schizophrenics, 10 delirium cases, 15 miscellaneous) were treated with an average dose of 3 mg haloperidol daily and EEG's were recorded for varying periods up to 3 months. No changes were registered in 10 cases, moderate changes in frequency and amplitude of basic activity were found in 8, improvement in the basic activity (with transitory and variable effects on the theta component) in 14 and retrogression was noted in 8 cases (both base activity and anomalous changes.) No epileptogenic effects were noted at the dosages used. The clinical symptomatic effects on the extrapyramidal system, the psyche and alertness were not reflected in the EEG's.

Hôpital Psychiatrique
Villejuif, Seine
France

2087 Borenstein, P., Dabbah, M., Blès, G., & Roussel, A. Etude électroencéphalographique de l'aminotryptiline. [Electroencephalographic study of aminotryptiline.] *Revue Neurologique*, 1962, 106, 225-237.

Clinical studies

Abstracts 2088-2090

Aminotryptiline was administered parenterally in doses of 100 mg once only to 57 patients, including 33 epileptics, 13 with behavioral disturbances, 7 depressed patients and 4 schizophrenics. Improvement was noted in 10 epileptics and retrogression (diffuse and bilateral point waves at 3-3.5 c/second) in 20 such cases; 10 nonepileptics showed improvement (regression of dysrhythmic points, etc); 5 cases of depression experienced an increase in amplitude and slowing of rhythm; effects on schizophrenics were variable. In 63 patients, including 21 epileptics, 35 with depression and 7 with behavioral troubles, all treated over a long period of time the results were as follows: during the first months the effect of aminotryptiline on the EEG tracings was variable, the most frequent phenomenon in depression being a retardation of basic activity concomitant with an increase of amplitude, while anomalous points appeared in the behavioral patients. Among epileptics isolated spikes, bilateral synchronous point waves, slowing in alpha rhythm, appearance of localized or diffused theta and delta elements occurred. Anomalies would vanish, then occasionally reappear. The drug cannot be viewed as epileptogenic as clinical improvement was frequent and anomalies were suppressed. Side effects consisted of anxiety symptoms and functional disturbances during the 1st days, asthenia, tremor, blurred vision, stammering, constipation, dry mouth, bulimia and considerable weight gain. Prognosis on an EEG-clinical basis is not yet possible.

Hôpital Psychiatrique
Villejuif, Seine
France

2088 Borenstein, P., Dabbah, M., Blès, G., & Roussel, A. L'aminotryptiline dans les épilepsies. Etude clinique et électroencéphalographique. [Aminotryptiline in epilepsy. A clinical and electroencephalographic study.] Annales Médico-Psychologiques, 1962, 120, 1, 153-167.

Aminotryptiline was administered, usually in oral doses of 50 mg t.i.d. to 23 epileptics (20 male, 3 female). The frequency of crises, psychomotor equivalents and absences decreased in 19 out of 23 cases, remained unchanged in 1, and retrogressed in 3 cases. Behavioral and character disorders were lessened in 14 cases. Subsequent treatment

of 2 patients with placebos resulted in reversion to the earlier condition. Injection of 100 mg aminotryptiline into 33 epileptics resulted in aggravation of the EEG's taken 30-180 minutes later in 20 cases, improvement in 10 and no change in 3. In nonepileptics with behavioral disturbances, EEG improvement was noted in 10 out of 13 cases. In 21 epileptic cases treated for 3 months with the drug, some EEG anomalies were noted at the start but these disappeared after the 1st month. Side effects were exceptional among epileptics, consisting of tremor, constipation, dry mouth, somnolence and some digestive disorders.

Hôpital Psychiatrique
Villejuif, Seine
France

2089 Frentzel, A., & Spazier, D. Über die Beendigung therapeutischer hypoglykämischer Komata durch Glucagon. [Termination of therapeutic hypoglycemia by glucagon. Der Nervenarzt, 1962, 33, 316-319.

Insulin shock was administered in 29 schizophrenic patients, with 35-750 U of insulin. Crystalline glucagon was used to terminate 1223 shocks (0.1 mg i.v. to 5 mg i.m.) Most patients responded within 5 to 20 minutes. The fastest response was achieved by i.v. administration, but was not related to insulin dosage, to duration or depth of the insulin shock. Delayed response (30 minutes) occurred 67 times, and 9 patients were unaffected by a second dose and had to be treated with glucose. Lack of response may be related to disturbances in potassium metabolism. No side effects were noted.

Psychiatrische und Neurologische Klinik
Universität Heidelberg
Heidelberg, Germany

2090 Heyck, H. Der Einfluss hochdosierter Dauerbehandlung mit Phenothiazinen auf den Hirnstoffwechsel bei verschiedenen Altersgruppen. Quantitative Messungen mit der Stickoxydulmethode. [The influence of prolonged treatment with large doses of phenothiazines on the brain metabolism in different age-groups. Quantitative measure-

ment with the nitrous oxide method.] *Der Nervenarzt*, 1962, 33, 66-70.

To determine cerebral blood flow and cerebral oxygen consumption in patients who received large doses of phenothiazine derivatives for a long time, 29 hospitalized patients, most with endogenous psychoses (23 aged 17-34 years and 6 aged 53-69 years) received perazine (300-1000 mg), Meller 1321 (350-500 mg), chlorpromazine (300 mg), piperazinoiminostilbene (800 mg) and levomepromazine (400 mg). The volume of brain-blood flow/100 g brain tissue/minute was calculated by the nitrous oxide method of Kety and Schmidt, as modified by Bernsmeier and Siemons. Results show remarkable differences in the two age groups. Patients under 50 years of age (average age 28.5 years) were compared with a control group of 20 healthy untreated patients (average age 28.2 years). No significant differences were observed in blood pressure, the volume of cerebral blood flow or the ratio of arteriovenous pressure. The cerebral oxygen consumption was identical in both groups. The cerebral glucose consumption of the phenothiazine-treated psychotics was slightly less than that of the healthy untreated individuals. In comparison with normal values, patients over 50 years of age showed elevated blood pressure; the volume of the cerebral blood flow was greatly reduced, the ratio of arteriovenous pressure was elevated and the cerebral oxygen consumption was depressed to a level usually seen only in severe intoxication and coma. The cerebral glucose consumption was also greatly reduced. Apparently, there is an age-dependent difference in the biological adaptation of CNS neurons under pharmacological stress. It is important to recognize the dangers inherent in administering large doses of phenothiazine-derivatives to people over 50 years old.

Psychiatrische und Neurologische Klinik
Freien Universität Berlin
Berlin, Germany

2091 Sattes, Hans. Therapeutische Möglichkeiten bei der Kombination eines zentralen Stimulans mit einem Neuroplegicum. Therapeutic possibilities with a combination of a central stimulant and a neuroplegic

agent.] *Der Nervenarzt*, 1962, 33, 86-88.

Clinical investigation with MF 11 d, an experimental drug which consists of piperazine-phenothiazine combined with a central stimulant, were simultaneously undertaken independently in 4 hospitals. Of 180 patients treated, 140 were schizophrenics, 19 had endogenous depressions, and 21 were treated for miscellaneous reasons. The daily dosage was 30-80 mg p.o., initially 10 mg t.i.d. or q.i.d. Most patients tolerated the drug very well. No significant effects were observed on the cardiovascular system. Blood counts and liver function tests showed no pathological changes. A distinct increase in weight was noted in most patients. The side effects were mostly parkinsonian in nature, and only occurred in 12-13%. The preparation is as efficacious as other piperazine-derivatives, but it is better tolerated. Patients generally become more responsive, and a distinctly beneficial psychomotor-activating effect may be observed. The results were very encouraging, particularly with catatonic schizophrenics. Therapeutic effects are equally valuable. Some patients however, proved resistant to the preparation.

Universitäts-Nervenklinik Würzburg
Würzburg, Germany

2092 Haase, H.J. Die Beeinflussung psychomotorischer Aktivität bei neuroleptischer und antidepressiver Behandlung. [The influence of neuroleptic and antidepressant therapy on psychomotor activity.] *Nervenarzt*, 1962, 33, 116-124.

The effects of chlorpromazine, prochlorperazine, fluphenazine and thioperazine (dosages: 438, 66, 13, 12, and 22 mg/day, respectively) on the behavior patterns of 96 predominantly schizophrenic patients were recorded for a period of 4524 days. The behavior of 39 patients with depressive psychoses, under treatment with imipramine, phenelzine, and nialamide was also recorded. Drug effects were measured with respect to increases and decreases in walking activity, and increases or decreases in speech and other activity. The relationship of these changes to the increase or decrease of akathisia was evaluated statistically.

Clinical studies
Abstracts 2093-2095

Neuroleptic drugs were found to have a distinctly more intense and direct effect than do the antidepressants on psychomotor activity; their influence appears to be exerted upon the extrapyramidal system.

Psychiatrische Klinik
Medizinische Akademie
Düsseldorf, Germany

2093 Mans, J., Cornil, & Ajzenberg. De l'interet de l'association systematique de la thiomucase aux neuroleptiques. [Significance of systematic combination of thiomucase with neuroleptics. *Annales Médico-Psychologiques*, 1962, 120, 1, 50-60.

A combination of the neuroleptic drugs (chlorpromazine, thiopropazine and levomepromazine) with thiomucase was injected i.m. into 37 psychiatric patients. When thiomucase is used in this fashion, the neuroleptic drugs diffuse very effectively, the beneficial clinical effect persists, and intraparenteral treatments can be continued for as long as the state of the patient renders it necessary. The pseudoinflammatory reactions, which hitherto had been a cause of difficulty when attempts were made to inject the drugs intramuscularly over longer periods of time, no longer occurred.

[No address]

2094 Gibbs, F.A., & Gibbs, E.L. Clinical and pharmacological correlates of fast activity in electroencephalography. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S73-S78.

Seventeen patients (16 schizophrenic and 1 mentally deficient) received chlordiazepoxide (60 mg/day), a chlordiazepoxide analogue (30 mg/day) or diazepam (30 mg per day) in randomized order for 10 days to determine therapeutic effects and EEG differences in waking and sleeping states. At effective dosages, the incidence of fast EEG activity was the same for all 3 drugs; 70% developed fast activity and 30% remained unchanged. No relationship was observed between EEG responses and thera-

peutic effect. Fast EEG activity appears merely a side effect. Clinical evaluation and EEG recordings were also obtained in 73 paranoids who received diazepam 30 mg/day. Of the 90 patients treated overall, 36% were clinically improved although their response was unrelated to EEG response. Side effects included dizziness, drowsiness or incoordination, and occurred in 20%.

Department of Neurology and Neurological Surgery
University of Illinois School of Medicine
Chicago, Ill.

2095 Towler, Martin L. The clinical use of diazepam in anxiety states and depressions. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S68-S72.

Twenty-two healthy control subjects aged 19-41 years received diazepam (15-50 mg per day until maximal tolerance was established, then decreased weekly by 5-10 mg/day until the drug was discontinued for 3 months. Exhaustive clinical and laboratory evaluations were performed including weekly EEG's. A definite change in EEG pattern was observed after 5-days of drug administration, but EEG patterns reverted to normal 3-4 days after diazepam withdrawal. Side effects included ataxia, drowsiness, slurring and impairment of speech, euphoria and a mild degree of apathy. Laboratory tests remained well within normal limits throughout the study. Subsequently, 17 patients with severe depression and 190 with mild depression aged 12-76 years, received diazepam (8-60 mg/day). Of the 17, 14 experienced excellent results, 0 good and 3 unsatisfactory. Of the 190, 48 had excellent results, 125 had good results and 17 were unsatisfactory. Overall, 187 patients improved and 20 did not. In a series of 20 patients suffering from anxiety states, responses were as follows: 9 excellent, 10 good and 1 unsatisfactory. Side effects paralleled those in control subjects and readily disappeared after reduction in drug dosage. Most patients who respond to diazepam manifest improvement within the last 2-3 days of therapy.

Neurology and Psychiatry
University of Texas Medical Branch
Galveston, Texas

Topeka State Hospital
Topeka, Kan.

2096 Feldman, Paul E. An analysis of the efficacy of diazepam. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S62-S67.

In the initial phase of a 2-part study, 30 anergic and 25 hyperergic patients, average age 35-36 years, received diazepam (2.5-5 mg t.i.d.) for an average of 97-102 days. A total of 9 evaluators participated in assessment procedures. Significant improvement was obtained by 50% of the anergic and 13% of the hyperergic group. Laboratory and clinical reports revealed that diazepam was nontoxic, produced mild, infrequent side effects, and was maximally effective at 20-30 mg/day. Beneficial responses were usually manifested between the 7th and 14th days of treatment. In the 2nd phase, 87 patients (17 with depressive reactions and 70 with anergic schizophrenia) average age 37 years, received diazepam (20-30 mg/day) for an average of 91 days. Seventeen evaluators assessed responses. Improvement occurred in 66% with depressive reactions and 58% with anergic schizophrenia. Symptoms ordinarily associated with anergia or depression (defects of accessibility, affect, participation in adjunctive therapy, etc.) responded most favorably to diazepam therapy. Comparison of reduction of target symptoms with diazepam and chlordiazepoxide revealed that hallucinations, hostility and combativeness remained unaffected by diazepam but were relieved to some extent by chlordiazepoxide. Chlordiazepoxide favorably influences sleep, appetite, hostility and combativeness, and generally acts as a sedative. Diazepam has a salutary effect on hypoactive patients and acts as an energizer. Diazepam, chlordiazepoxide, an MAO inhibitor and one of the phenothiazines were compared for effects on a selected group of target symptoms (affect, tension, hallucinations, etc.). Diazepam was similar activity-wise to the energizers. Neither diazepam nor chlordiazepoxide was efficacious in the range of activity encompassed by the phenothiazines. Side effects included mild hypotension, dizziness, constipation and incontinence.

2097 Sargent, William. The treatment of anxiety states and atypical depressions by the monoamine oxidase inhibitor drugs. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S96-S103.

Sixty patients with anxiety states received a combination of MAO inhibitors [(isocarboxazid, phenelzine, phenoxypropazine or iproniazid) dosages unspecified] and chlordiazepoxide, MAO inhibitors alone or chlordiazepoxide (10 mg b.i.d. or t.i.d.) alone. Fifteen patients, average age 41 years, responded best to MAO inhibitors alone. Good previous personalities characterized 87% of these patients, and precipitating factors were present in 73%. Severe depression was present in 13% and mild depression in 87%. Of the 28 patients, average age 42 years, who responded optimally to MAO inhibitors and chlordiazepoxide, 75% had good previous personalities and 43% had precipitating factors. Hysterical behavior was present in 43% and mild depression was manifested by 97%. Of the 17 patients, average age 41 years, who failed to respond to MAO inhibitors and chlordiazepoxide, only 25% had good previous personalities and 29% had adequate precipitating factors. Hysterical behavior was seen in 23%, but mild depression was observed in 94%. All patients who initially responded well to a combination of MAO inhibitor and chlordiazepoxide showed a return of symptoms when the MAO inhibitor was withdrawn and the patient was maintained on chlordiazepoxide alone. An MAO inhibitor combined with chlordiazepoxide will ameliorate cardiac neuroses, effort syndrome and hysterical hyperventilation syndrome within 7-10 days in patients so predisposed.

Department of Psychological Medicine
St. Thomas's Hospital
London, Great Britain

2098 Freund, J. Dennis. The place of insulin coma therapy in modern psychiatry. *Journal of Neuropsychiatry*, 1962, 3, 246-250.

Clinical studies
Abstracts 2099-2101

A series of 2033 patients (71% paranoid schizophrenic, 14% catatonic, 5% pseudo-neurotic, 8% schizoaffective and 2% miscellaneous) received insulin coma therapy. Results included full recovery in 1402 (69%), great improvement in 183 (9%), improvement in 102 (5%) and no improvement in 346 (17%). Of the 346 who failed to improve, 189 received ECT superimposed at the deep coma level. Of the 189, 168 (89%) recovered fully and 158 (11%) did not improve. A plethora of references allude to work done with insulin coma therapy since 1937.

Fairview Hospital
2828 South Prairie Avenue
Chicago, Ill.

2099 Mans, J., Cornil, J., & Ajzenberg, D. Essais thérapeutiques du G. 22-355 chez les vieillards d'un service psychiatrique. [Therapeutic trials with G. 22-355 (imipramine) in older patients in a psychiatric clinic] *Annales Medico-Psychologiques*, 1962, 120, 2, 57-70.

Imipramine was administered to 41 geriatric patients, at an initial dose of 110 mg tablet per day, gradually increased to 5 or 6 per day according to the age of the patient or the gravity of the syndrome. The patients were classified as follows: 30 pure seniles, 4 premature seniles, and 7 miscellaneous cases with psychasthenia, depression, melancholia, in all of whom the depressive or melancholy aspect was dominant. Imipramine proved effective in combating emotional phenomena consisting of outbursts of laughing or weeping, in calming paranoids and depressives, while poor or indifferent results were registered in hypochondriacs and senile dementia cases. Generally speaking, advanced cases do not respond, while in less advanced cases contact is made easier, and the troubles of the patient become less painful.

[No address]

2100 Lairy, G. C. Action du Librium sur l'électroencéphalogramme. [Action of Librium (chlordiazepoxide) on the encephalogram.] *Révue Neurologique* 1962, 106, 152-156.

EEG's of patients at rest but awake show very slight changes under i.v. or oral administration of 30-50 mg/kg chlordiazepoxide, these consisting mainly of a decrease in amplitude and increase in frequency of the alpha waves and some reduction of the theta component. Effects are likewise slight during the sleep cycle, consisting of some increase in high-frequency components, particularly the 14 c/s spikes. No pathological aspects were noted, nor was there any suppression of physiological stages. Doses of 50 mg/kg i.v. have a clearcut effect on intermittent photostimulation. The EEG tracing shows suppression of oculo-clonic charges through recruitment, when, simultaneously, suppression of clinical and subjective reactions occurs.

Institut National d'Hygiène
Paris, France

2101 Kammerer, T., Geissmann, P., Wartel, R., & Levy, A. Etude clinique, biologique et électroencéphalographique de l'action du KT 5 (Keithon) dans certains syndromes psychiatriques. [Clinical, biological and electroencephalographic study of the action of KT 5 (Keithon) in certain psychiatric syndromes.] *Annales Medico-Psychologiques*, 1962, 120, 1, 119-130.

Phenoxethamine (KT 5) was administered to psychiatric patients t.i.d., up to a maximum of 300 mg per day in the form of 50 mg tablets. Out of 8 demential, depressive, and asthenic psychotics, 4 did not improve at all, 3 improved moderately and 1 was considerably helped. Out of 7 psychoneurotic patients, 3 clearly improved, 2 were partially better, and 2 did not improve. Out of 10 neurotic depressed patients with marked asthenia, there were 2 failures and 8 either partial or complete successes. Out of 5 posttraumatic neurotic patients 4 were partially improved. On the whole demential or psychotic patients or psychopaths who were not depressed are not favorably affected by phenoxethamine, whereas depressed patients are amenable to treatment. Obsessional psychoneurotics do not respond, while those suffering from phobias do undergo improvement. Side effects are variable and not directly related to the quantity administered. They generally con-

ist of somnolence and fine tremors of the limbs. Biological constants are not affected, but the EEG shows some changes when the clinical response is favorable, these changes consisting generally of a slowing-down of alpha rhythm and an occurrence of slow waves, which sometimes are generalized.

Institut National d'Hygiène
Paris, France

2102 Salera, Adolfo. La nialamida en el tratamiento de los estados depresivos de diversa etiología. [Nialamide in the treatment of depressive states of various etiology.] *Semana Médica*, 1962, 121, 1207-1208.

One-hundred-and-five patients, seen in private practice, including 32 cases of reactive depression, 22 simple depression, 21 schizophrenic depression, 13 menopausal depression, 10 schizoid depression and 2 reactive neurosis, were treated with 8 tablets of nialamide daily for 10 days. Dosage was lowered when signs of success were noted. Rauwolfia (with or without hormones) was often used concomitantly and 27 of these patients received ECT (4-8 applications). Excellent results were obtained in 22, very good results in 54, fair improvement in 15, no change in 5 and no effect in 9. Of 32 patients with reactive depression, 31 benefited with treatment. Of 13 with menopausal depression, 11 showed improvement.

No address]

2103 Martin, F., & Charghi, A. 5 La crise électro-clinique à la Megimide et l'activation de l'électroencéphalogramme par quelques sédatifs et hypnogènes: Etude comparative chez l'épileptique. [The electro-clinical crisis under Megimide (bemegride) and activation of the encephalogram by several sedatives and hypnogenics. A comparative study of epilepsy.] *Schweizer Archiv für Neurologie, Neurochirurgie und Psychiatrie*, 1962, 89, 72-93.

Twenty-three epileptics, 14-57 years old, had EEG's recorded after pentothal (2.5% solution up to a maximum of 20 cc i.v.), alpha-chloralose per os (0.45-0.75 g), methyprylon (5% solution i.v. with maximum

of 20 cc), and bemegride (0.5% solution - dose of 1 cc/10 kg, followed by 1 cc at 15 second intervals up to 100 cc maximum). The epileptic crises were filmed simultaneously with the recording of the EEG tracing. Comparative studies on the different activation and provocation techniques show considerable variation between the patterns evoked by different techniques. Even when it is known that a definite cortical and hemispheric pathology is present, proof of a definite epileptogenic focus is very chancy. Presence of a well-defined electrical focus which would permit good electro-clinical correlation is found in a very small number of cases, and is rendered difficult to ascertain by the differences between the different methods. Results presented here are of importance in the sense of demonstrating the need for sharpening techniques and methods for determining by means of electro-clinical correlation, the epileptogenic focus.

Laboratoire d'Electroencéphalographie
Hôpital Cantonal de Genève
Geneva, Switzerland

2104 Detre, Thomas P., Feldman, Robert, G., Rosner, Burton, & Ferriter, Christine. Vibration perception in normal and schizophrenic subjects. *Journal of Neuropsychiatry*, 1962, 3, 145-150.

Vibrograms were traced by 9 acute schizophrenics, aged 18-30 years, and 31 normal controls employing the principle of the Bekesy audiometer in which the subject automatically traced his own threshold of vibration perception. No significant differences were observed in audiograms between normal and schizophrenic subjects. The average threshold of vibration perception was highest for the female schizophrenics and next highest for the schizophrenic males. Both were appreciably higher than the threshold curves for normal males and females. As a control measure, audiograms and vibrograms were determined over the same frequency range on 2 normal and 2 schizophrenic subjects. The normal and schizophrenic subjects had comparable audiograms while the vibrograms of the schizophrenics were distinctly different from those of the normals. Serial tests were

Clinical studies
Abstracts 2105-2107

used to show the effects of fluphenazine and trifluoperazine on vibratory sensitivity. Minimal changes occurred in threshold curves when normal subjects received the drugs, but definite changes occurred in serial vibrograms of drug-treated schizophrenics. Clinical improvement was reflected in a shift of the average vibration threshold into the normal range. The audiometric vibrogram may be useful in evaluating psychopharmacological drugs.

Department of Psychiatry
Yale University School of Medicine
New Haven, Conn.

2105 Lohrenz, John G., Levy, Leonard, & Davis, John F. Schizophrenia or epilepsy? A problem in differential diagnosis. *Comprehensive Psychiatry*, 1962, 3, 54-62.

A 4-year-old girl with acute schizophrenia and epilepsy received chlorpromazine (200 mg/day), diphenylhydantoin (100 mg t.i.d. with a maintenance dose of 100 mg/day) and phenobarbital (60 mg parenterally). Aberrant EEG tracings necessitated maintenance therapy with diphenylhydantoin. The significance of the EEG in differentiating between epilepsy and schizophrenia is stressed as well as the importance of conservative management in such atypical cases. Maintenance therapy aided complete recovery. A brief survey of pertinent literature is included.

Department of Psychiatry
McGill University
Montreal, Quebec
Canada

2106 Keller, Hans H. Ein weiterer Beitrag zur medikamentösen Parkinson-Therapie. [A further contribution to the drug therapy of Parkinson's disease.] *Münchener Medizinische Wochenschrift*, 1962, 104, 510-513.

The effect of thenophenopiperidine (Sandosten) was measured separately for each of a series of 11 symptoms of Parkinson's disease. Results are based on 30 patients, but additional studies confirm these findings. Treatment consisted of oral or i.v. administration of thenophenopiperidine (2

tablets t.i.d.) or Sandosten-calcium (1 tablet t.i.d.) or a combination of both, for a period of 14-28 days. Results proved significant for the somatic symptoms (e.g., tremors, posture, etc.), but not for the psychomotor symptoms. The drug is tolerated even with patients who do not tolerate other drugs or who experience side effects from other medication. No side effects were noted.

Nervenklinik
Universität München
München, Germany

2107 Bauer, A., Klinische Erfahrungen mit Thioridazin (Melleril-Sandoz) anhand von 202 Fällen, zugleich ein Beitrag zur Problematik der Behandlung endogener Depressionen. [Clinical experience with thioridazine (Melleril-Sandoz) based on 202 cases together with a contribution to the problem of treating endogenous depression.] *Nervenarzt*, 1962, 33, 321-324.

In a 9-month period, 202 clinical patients were treated for an average of 3-5 weeks with doses of 400-500 mg/day thioridazine. In a few cases the doses were as high as 1600 mg/day. Of these patients, the majority (129) were suffering from endogenous depressions; 52 (40%) were considered greatly improved, 47 on thioridazine alone and 5 on thioridazine plus imipramine or ECT. Forty-one (32%) showed moderate improvement, 33 on thioridazine alone and 8 receiving thioridazine plus imipramine. The remaining 36 patients (28%) were either unimproved or treatment was interrupted because of complications (8 patients). Of 36 patients with situational depressions, 1 were cured with complete disappearance of depressive symptoms, 11 showed marked improvement, and 1 remained unimproved. Unequivocal improvement resulted with discharge after 3-4 weeks on a maintenance dose in 10 of 12 manic-depressive patients. The drug was also used in 35 schizophrenics in mild states and in patients who were only occasionally hallucinating. These patients were treated for 6-8 weeks until hallucinations lessened.

Nervenklinik der Stadt und Universität
Frankfurt-am-Main, Germany

2108 Helbig, Hans, Das tödliche Alkohol-delir, darestellt an 54 Fällen. [Fatal alcohol delirium, presentation of 54 cases.] Nervenarzt, 1962, 33, 221-226.

Statistical analysis of 54 fatalities indicated that the number of lethal outcomes of alcoholic delirium is not dependent upon therapy. Three types of therapy were employed singly and in combination: sedation (principally paraldehyde); cardiac and circulatory treatment, and supportive liver therapy (vitamins, etc.). There was no correlation between type of therapy and death.

Karl-Bonhoeffer-Heilstätten
Berlin-Wittenau

2109 Burchard, Johann M. Klinisch-psychiatrische Erfahrungen mit Triptizol. [Clinical psychiatric experience with Tryptizol.] Nervenarzt, 1962, 33, 319-321.

Forty-five male clinical patients were given amitryptiline (Tryptizol) usually orally, though in a few cases by i.m. for 8-93 days (average 28 days), at a dose of 150 or 225 mg daily in 37 cases. The lowest effective dose was 75 mg/day, the highest 400 mg/day. During amitryptiline treatment, all other therapy with the exception of barbiturates was stopped. Ten of 13 cases of endogenous depression were markedly improved, 3 slightly improved. Of 11 other depressive disorders, 7 were markedly improved, 2 slightly improved, 2 unchanged. Of 4 manic depressives without paranoid hallucination syndrome 1 was considerably improved, 3 were slightly improved. Three of 4 manic depressives with paranoid hallucinations were considerably improved, 1 slightly improved. Six schizophrenics were either slightly or markedly improved, 2 were unimproved and 1 became worse. Of 3 patients with organic disease, 1 was markedly improved, 1 slightly improved and 1 unimproved. One patient with chorea was unaffected. Half of the treated patients developed tachycardia, but extrapyramidal symptoms, except for a slight finger tremor in 1 patient, were absent.

Psychiatrische und Nervenklinik
Universität Hamburg
Hamburg, Germany

2110 Tölle, Rainer, Die Behandlung endogener Psychosen mit Laevomepromazin (Neurocil). [Treatment of endogenous psychoses with levomepromazine (Neurocil).] Nervenarzt, 1962, 33, 178-180.

Eighty-three female patients with acute schizophrenia, hebephrenia, defect schizophrenia and manic psychoses were given levomepromazine orally 150-250 mg/day, in severe cases 400 mg, rarely 500 mg/day (generally only 2/3 of the dose of chlorpromazine required to give the same effect). The treatment was ineffective in 11 acute schizophrenics with paranoid hallucinations, but was effective in 4 patients with considerable motor unrest but without delusions; it was very effective in the control of convulsions. In 13 acute schizophrenics with hebephrenic symptoms 400-500 mg/day was necessary; results were good in 6 cases, moderate in 4, negligible in 3, and generally were evident in 2-3 weeks. Results were convincing in only 6 of 22 patients with defect schizophrenia and were unfavorable in patients requiring continuous treatment, because of the exhausting effects of levomepromazine. The drug, 100-200 mg/day orally (initially 75-100 mg i.m.) favorably influenced the anxiety states of 10 patients (5 schizophrenic, 5 cyclothymic) and inhibited delusions. It was relatively ineffective in 7 depressed patients; only 3 patients were improved by high doses of about 400 mg/day. Four cyclothymic-depressed patients were unimproved. Treatment of 5 manic psychoses (3 cyclothymic, 2 miscellaneous psychotics) with levomepromazine gave good results. The principal side effect was a pronounced decrease in blood pressure resulting in collapse in hypotonic patients and those with low blood pressure. In general levomepromazine was less effective in acute and chronic schizophrenia than the piperazine phenothiazine derivatives.

Universitäts Nervenklinik
Tübingen, Germany

2111 Schmidt, & Van Ba, Nguyen. Traitement d'un malade par le prothipendyl C.I.H. [Treatment of a patient with prothipendyl C.I.H.] Annales Médico-Psychologiques, 1962, 120, 1, 147-152.

Clinical studies
Abstracts 2112-2114

A 25-year-old male was admitted with delirium of several weeks duration. He was given 50 mg chlorpromazine by injection, followed by t.i.d. oral chlorpromazine, then 10 ECT sessions. Several weeks after such therapy the patient was switched to prothipendyl beginning with i.m. injections of 80 mg. Then injections were alternated with 50 mg tablets, later 50 mg prothipendyl tablets t.i.d. The patient showed good recovery within 2 weeks.

[No address]

2112 Náhunek, K. Die Behandlung endogener Depressionen mit Perphenazin und Trihexyphenidyl. Beziehung zur extrapyramidalen Symptomatologie. [Treatment of endogenous depression with perphenazine and trihexyphenidyl. Relationship to extrapyramidal symptomatology.] Acta Psychiatrica Scandinavica, 1962, 38, 108-116.

Sixty-eight patients with melancholia and involutional depression were treated with perphenazine or trihexyphenidyl on 1 of 3 dosage schedules. The 1st group of 26 patients was given 24-96 mg perphenazine and 6-12 mg trihexyphenidyl a day for 16-38 days. The 2nd group of 26 patients received perphenazine alone, 24-76 mg/day for 5 to 33 days; the 3rd "control" group of 16 patients received trihexyphenidyl alone (6-12 mg/day for 3-14 days). In the event of failure of treatment in the 2nd and 3rd groups, trihexyphenidyl was added to the treatment of the 2nd group and perphenazine to the 3rd. Results were evaluated by 2 doctors according to a modified Serejski classification as cured, markedly improved, partially improved, insignificantly improved, unimproved, or worsened. In the 1st treatment group who received the 2 drugs in combination, 16 patients were discharged, 4 were partially improved and 6 were unchanged. In the 2nd group, trihexyphenidyl was given to 23 patients when perphenazine proved ineffective; 3 of the patients were discharged on perphenazine alone and 13 when trihexyphenidyl was added. Nine patients improved partially with the drugs in combination, 1 slightly, 1 was unchanged and 2 were worsened. Of 16 patients who at first received only trihexyphenidyl, there was only 1 who showed slight

improvement, but when perphenazine was added to the treatment, 8 were discharged, 4 were partially improved, 2 slightly improved and 3 were unchanged. A correlation could be demonstrated in the 1st 2 group between good therapeutic results and absence of extrapyramidal symptoms on the one hand, and poor results and the presence of extrapyramidal symptoms on the other hand.

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2113 Lindner, Manfred, "Über vorbeugende Dauerbehandlung von Depressionen. Eine vorläufige Mitteilung. [Prophylactic chronic treatment of depressions. Preliminary report.] Nervenarzt, 1962, 33, 177-178.

A total of 62 private ambulatory patients, suffering from various forms of depression, 17 with periodically recurring depressions (5 reactive depression, 3 involutional depression, 9 endogenous depression) were treated with small doses of imipramine of 25-150 mg/day for 9-28 months. These were in addition to the much higher therapeutic doses given initially which varied from 100-300 mg/day, 1 patient receiving as much as 400 mg/day. In 14 out of the 17 cases, the frequency, severity and duration of individual spells of depression were favorably affected; in the 3 others the severity of depression was reduced. Three brief case histories are presented: 2 cases were almost completely relieved of depression after perphenazine treatment and chronic imipramine treatment; a 3rd was controlled with imipramine and phenothiazine given for a periodically recurring hypomania. There were no significant side effects attributable to this therapy.

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2114 Von Brauchitsch, Hans, Die klinische Wirkung des Benzoquinolizinderivates Nitoman bei der chronischen Schizophrenie. [Clinical effect of the benzoquinolizine derivative Nitoman in chronic schizophrenia.]

Nervenarzt, 1962, 33, 60-66.

One-hundred-and-thirty-four hospitalized patients, 104 of whom were schizophrenics, refractory to other forms of treatment including shock therapy, phenothiazines and sleep therapy, were treated initially with 50 mg/day of tetrabenazine (Nitoman) orally, which was increased to 250 mg/day or decreased to as little as 75 mg/day depending on side effects in the individual patient. Results were evaluated as follows: O, patient's condition unaltered or worse; I, slight improvement in ability to work and adaptation to surroundings, but still confined to a closed ward; II, marked improvement, with transfer to a convalescent ward; III, improved to the extent of discharge. Of the 104 schizophrenics, 22 were discharged, 9 were placed in Group II, 32 in Group I and 60 were in the O category. Hebephrenic patients responded the best to tetrabenazine treatment, catatonics less well, while paranoids showed little response. Tetrabenazine was also effective in 3 cases of abnormal reaction (1 patient in Group II, 2 in Group I) and in 3 cases of alcoholism (2 in Group II and 1 in Group I). Four of 11 patients with organic psychoses were improved slightly and 1 discharged. Of 13 manic depressives, 7 were unimproved, while 2 were placed in each of the improved categories. Tetrabenazine compared favorably with other therapeutic agents, particularly with respect to the number discharged. When results were broken down

on the basis of duration of treatment, the drug appeared to be optimally effective at about the 3rd week of treatment. The most common side effects were malaise, pulse irregularities, hypothermia, Parkinsonism (resulting in cessation of treatment in 7 patients), nausea and vomiting (treatment discontinued in 5), insomnia, turbulence (discontinued in 10), convulsions (discontinued in 9), collapse and depression.

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2115 Baruk, H., & Richardeau. Traitement d'un cas grave de dépersonnalisation avec troubles de la conscience par la phénelzine. [Treatment of a serious case of depersonalization with intellectual disorders with phenelzine.] *Annales Médico-Psychologiques*, 1962, 120, 1, 950.

A male patient suffering from depersonalization, perceptual disorders (lack of time appreciation, etc.) and amnesia, who had an abnormal EEG, was greatly aided by treatment with phenelzine [no details].

[No address]

See also 1989, 2120, 2168, 2208, 2225, 2234

SIDE EFFECTS

2116 Rabinowicz, Th., & Foroglou, G.P.
4. Lésions par intoxication aiguë à l'imipramine. [4. Lesions caused by acute imipramine intoxication.] Schweizer Archiv für Neurologie, Neurochirurgie und Psychiatrie, 1962, 90, 268-295.

A 59-year-old woman who had previously been given ECT for depression committed suicide through the ingestion of 182 25 mg imipramine tablets. In the past, 1 of her brothers and a sister had committed suicide. Two days before her death she had begun treatment with 9 tablets per day. Ten hours after the toxic ingestion she was found unconscious and entered the hospital in a deep coma with total areflexia and a drop in blood pressure; she died within 8 hours, having epileptic seizures. Imipramine levels in body fluids and organs were (in mg%): plasma 0.2; urine 0.7; bile 3.2; gastric contents 810; intestinal contents 108; intestinal walls 5.1; heart 5.0; liver 23.0; spleen 40.5; muscles 3.5; kidneys 9.50; thyroid 2.0; adrenals 17.6; brain (average of 560 g): 11.3; gyrus centralis 10.7; nucleus caudatus 12.4; brain stem 11.1; frontal lobe 10.3; basal ganglia 13.1; temporal lobe 11.2; occipital lobe 10.0; pons 12.6; thalamus 12.8; cerebellum 3.2. In the CNS (lower brain stem and spinal cord were not available), the left side was used for histological examination, and severe lesions probably caused by the product were found in the following regions: putamen (partly), claustrum (partly), large neurons of the nucleus caudatus, nucleus ruber, nucleus parasympathicus of the 3rd cranial nerve, nucleus oculomotorius (III), nucleus motorius trigemini, olivae bulbaris, certain hypothalamic and thalamic nuclei and certain elements of the reticular system. The following regions were less severely involved: anterior part of the gyrus uncinatus, a small part of the reticular substance of the pons and certain thalamic and hypothalamic nuclei. A list of nuclei with slight lesions (probably due to hypoxemia following circulatory and/or respiratory failure) is presented.

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2117 Bui Quoc Huong. Multinévrite secondaire à une intoxication massive par le méprobamate. [Polyneuritis due to massive intoxication with meprobamate.] Revue Neurologique, 1962, 106, 325.

A 19-year-old girl ingested 14.4 g meprobamate and became comatose for 60 hours. On regaining consciousness she had a motor sensitive polyneuritis of the legs, particularly the left leg. The polyneuritis lasted several months.

[No address]

2118 Müller, D., & Glatke, E. Über eine Phenothiazin- [N-(2-Dimethylamino-propyl)-phenothiazin-hydrochlorid- "Prothazin"]- Intoxikation mit Delir bei einem 5 jährigen Mädchen. [Intoxication with delirium in a 5-year-old girl caused by the phenothiazine: N-(2-dimethylamino-propyl)-phenothiazine-HCl- "Prothazin."] Psychiatrie, Neurologie und Medizinische Psychologie, 1962, 14, 54-59.

A 5 1/2 year old girl showed delirium after ingesting 200-300 mg promethazine (Prothazin). An alpha rhythm of 10/second with dysrhythmia was noted in the EEG. The child initially had a temperature of 38.3° C and a pulse of 160/minute. She fully recovered within 24 hours without complications following symptomatic treatment.

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2119 Croughs, R.J.M., Le Poole, A., & Ten Bokkel Huinink, S.A. Interstitiële nephritis waarschijnlijk door het gebruik van fenacetine. [Interstitial nephritis probably due to phenacetin habituation.] Nederlands Tijdschrift voor Geneeskunde, 1962, 38, 1899-1902.

Chronic interstitial nephritis was diagnosed in a woman who, at rough estimate, must have ingested approximately 12 kg of phenacetin over a period of 25 years. In any case of unexplained anemia or renal dysfunction, it is advisable to inquire into

the possible abuse of analgesics.

Interne Afdelingen van het Gemeente-
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Rotterdam, The Netherlands

2120 Jacobziner, Harold. Poisonings associated with tranquilizers. *Clinical Pediatrics*, 1962, 1, 16-18.

During the 1st 6 months of 1962 the New York City Poison Control Center reported more than 300 incidents associated with the ingestion of tranquilizers. Twenty incidents with moderate to severe side reactions were reported due to 1 product alone. The victims ranged in age from 1-49 years; 2 were children under 15 years. At least 35 different tranquilizers are currently available. Individuals taking tranquilizers may suffer impairment of psychomotor performance even with moderate doses. Other well known effects such as parkinsonism, jaundice, agranulocytosis, etc. are cited. The fact that thalidomide was not approved for commercial distribution is noted as due to the alertness of Dr. Kelsey. Thalidomide in doses as little as 72 mg/day taken in the 2nd week of pregnancy may induce teratogenic anomalies. A table is

presented showing a sample of poisonings reported in New York City on 1 weekend.

[No address]

2121 Schmitt, Alfred. Besonderheiten bei Vergiftungen mit "barbitursäurefreien" Schlafmitteln. [Characteristics of poisoning with "barbiturate free" sleeping potions.] *Nervenarzt*, 1962, 33, 418-419.

Relatively small amounts (20-30 tablets) of the so-called barbiturate-free drugs, including glutethimide, methyprylone and methaqualone have deleterious effects on circulation often greater than those caused by the barbiturates. A specific effect of glutethimide is an increase in the likelihood of convulsions. Four suicide attempts are described in which methaqualone was the drug taken, 2 of them with fatal outcome. In each case 40-100 of these tablets were taken. Symptoms included edema of the lung, severe oxygen insufficiency, heart and circulatory failure.

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See also 1988, 1991, 2046, 2154, 2158, 2159, 2161, 2171, 2173, 2190, 2197

2122 Dostalek, C., & Scheer, E. Über den Einfluss von Benactyzin und Atropin auf die bedingten Pupillenreflexe bei Katzen. [The influence of benactyzine and atropine on conditioned pupillary reflexes in cats.] *Acta Biologica Medica Germanica*, 1962, 8, 523-529.

Conditioned pupillary reflexes were formed in 5 cats. Light exposure of 1 eye served as a US which produced maximal miosis, while a tone was used as a CS. This sound stimulation did not effect any change of the pupils before the formation of a CR, not even when applied at 10-fold amplitude. During and after formation of the conditioned miosis, mydriasis also occurred. Atropine (25 µg/kg) and benactyzine (100 µg/kg), s.c., eliminated or reduced mydriasis and promoted the formation of the conditioned miosis. Here atropine caused a light miosis. The effects of atropine and benactyzine on the pupillary CR's were contrary to the effect upon the peripheral target organ.

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Berlin, Germany

2123 Pihkanen, T., & Kauko, O. The effects of alcohol on the perception of musical stimuli. *Annales Medicinæ Experimentalis et Biologiæ Fenniae*, 1962, 40, 275-285.

Three blind piano tuners, 2 men and a woman, were tested for ability to determine pitch, loudness, rhythm and for tonal memory after the ingestion of alcohol. The dosage of ethanol was 1 g/kg given as a 20% solution in 2 divided doses: the 1st dose (0.75 g/kg) was taken slowly in the 1st hour and the 2nd (0.25 g/kg) during the 2nd hour. The Seashore Measures of Musical Talent was used in evaluation. The same subjects were given the test again a week later when sober for comparison. Alcohol caused disturbances in pitch and rhythm perception, and in tonal memory, but no distinct effect in respect to loudness perception.

Institute of Occupational Health
Helsinki, Finland

2124 Ekström, Nils Åke, & Sandberg, Finn. A method for quantitative determination of the inhibitory effect on the conditioned avoidance response of mice. *Arzneimittel-Forschung*, 1962, 12, 1208-1209.

Female mice were conditioned to avoid a shock (escape response) delivered from a grid floor which was accompanied by a buzzer tone. Three to five conditioning trials were made on each of 15 consecutive days, after which an escape response was elicited by the buzzer tone alone. From a group of 100 CAR mice the 50 best ones were chosen for further training which was continued until 80% had a reaction time of less than 3 seconds in 5 consecutive trials. Groups of 10 were used for each of the 5 drugs tested and reaction time was determined before and 45 minutes after i.p. drug administration. The drugs used were, in mg/kg: chlorpromazine 1.25-10.00, perphenazine 0.3-8.1, promazine 2.0-16.0, amphetamine 0.5-4.0 and H 2/13 25.0-100.0. The latter is 5-exoethyl-2-norbornene-5-endocarboxamide. All drugs except amphetamine decreased the percentage of CAR's. Amphetamine failed to enhance the conditioned response. ED 50's were in mg/kg: chlorpromazine 4.85, perphenazine 2.27, promazine 5.00 and H 2/13 53.5.

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2125 Goldberg, H.D., Peck, R.E., Chappell, M.N., & Lipinski, C.E. Effect of carbon dioxide on anxious behavior in the rat. *Journal of Neuropsychiatry*, 1962, 3, 390-392.

Rats trained to press a bar for a food reward received EST to induce conditioned suppression, after which 4 control rats and 4 experimental animals (previously deprived of food for 23 hours, placed in Skinner boxes equipped with bar presses) received EST, followed by compressed air or CO₂ hosed into the cages of the experimental animals for 30 seconds. The CO₂ induced initial attitude of alertness followed by excessive hyperpnea and coma. Within 30 seconds, CO₂ treated rats were frolicsome, and returned to bar-pressing.

in 30 minutes, 1/3 the time required for control animals. In addition the experimental animals bar-pressed 13 times more often in the succeeding hour than did the controls. In confirmation of the original hypothesis, CO₂ discharged anxiety from the body, thus enabling the rat to continue pre-anxious behavior. An alternate explanation promulgates the theory that CO₂ produced a retrograde amnesia obliterating the original unpleasantness associated with EST.

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2126 Morgenstern, F.S., Beech, H.R., & Davies, B.M. An investigation of drug induced sensory disturbances. *Psychopharmacologia*, 1962, 3, 193-201.

Eighteen healthy volunteers, aged 20-40 years, were studied in relation to psychological disturbances produced by phencyclidine (7.5 mg tablets). Six were control subjects, the rest experimental. Testing began immediately after the 1 ingested dose. Perimetry, audiometry, visual acuity, taste threshold (quinine), touch, point discrimination and position sense were tested. This battery was administered every 15 minutes and took 10-12 minutes to complete. Controls were tested for 2 consecutive hours and experimental subjects were tested continuously until their test performance had returned to near normal. Results appeared to support the contention that the symptoms produced by the drug may be a result of partial sensory deprivation. The sensory changes tended to occur well in advance of psychological disturbance, i.e., most subjects were already showing impairment of sensory thresholds before verbal reports of "lightheadedness", "a slightly drunken feeling", etc.

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2127 Geller, Irving, Kulak, John T., Jr., & Seifter, Joseph. The effects of chlor-

diazepoxide and chlorpromazine on a punishment discrimination. *Psychopharmacologia*, 1962, 3, 374-385.

Male Holtzman-Sprague-Dawley strain rats were conditioned to a punishment discrimination by simultaneously rewarding with food and punishing with shock, all lever responses made in the presence of a discriminative stimulus (tone). Shock intensity was either high or low, but stable during the tone periods. Various doses of each drug were administered i.p. in intervals of at least 2 weeks. On the high-shock control baseline, rats were given chlordiazepoxide in doses of 7.5, 15.0 and 30.0 mg/kg. These worked during tone periods and tolerated more shocks at 7.5 and 15.0 mg/kg, while 30 mg/kg produced side effects interfering with performance. On the low shock baseline, rats were given chlorpromazine in doses of 0.25, 0.5, 1.0, 2.0 and 3.0 mg/kg; these accepted less shocks during the tone period with a decrease in shocks related to an increase in dosage. This technique may be useful in investigating new compounds before clinical investigations.

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2128 Scriabine, A., & Blake, M. Evaluation of centrally acting drugs in mice with fighting behaviour induced by isolation. *Psychopharmacologia*, 1962, 3, 224-226.

Aggressive male mice in which fighting behavior was induced by isolation, were used in pairs to compare the tranquilizing activity of chlorpromazine, chlordiazepoxide and meprobamate at 3 dose levels. Reduction in fighting time for pairs of mice was used for evaluation. Dose increase, limited to the level at which motor function was impaired, was comparable for mice treated with 4-8 mg/kg chlorpromazine, 20 mg/kg chlordiazepoxide and 200 mg/kg meprobamate i.p. Highest reduction in fighting time occurred with chlorpromazine and lowest with chlordiazepoxide. As an antifighting agent, chlorpromazine was 13.1 times more potent

than chlordiazepoxide, and the latter was 8.3 times more potent than meprobamate. This method is considered efficient and precise for quantitative evaluation of potential tranquilizing agents.

Department of Pharmacology
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Groton, Conn.

2129 Grandjean, E., Battig, K., & Wanner, H.U. Die Wirkungen eines Narkotikums (Trichloräthylen) auf verschiedene Verhaltensreaktionen der Ratte. [The effect of an anesthetic (trichlorethylene) on various behavioral responses in rats.] *Helvetica Physiologica et Pharmacologica Acta*, 1962, 20, C25-C26.

The effect of inhalation of trichlorethylene vapors (200-1600 ppm, 4-8 hours/day for up to several months) on CAR's, swimming time, performance on Hebb's intelligence test, the climbing test and the T-maze, and spontaneous motility was studied in rats. At 200-800 ppm, sedative effects predominated under most test situations, but some tests revealed decreased inhibitions or increased motivation. At 1600 ppm, the effects were almost all sedative in nature.

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2130 Peterson, Ernest A., Haun, Kenneth, & Upton, Morgan. The effects of meprobamate, d-amphetamine, and placebo on disjunctive reaction time to taboo and nontaboo words. *Psychopharmacologia*, 1962, 3, 173-187.

To compare the effects of meprobamate and dexamphetamine, a study was made of response to lists of frequently occurring nontaboo words and taboo words, all of the same length and classifiable under animal, vegetable or mineral categories. Following a study of the response of 19 healthy males without medication, 72 subjects were tested in 12 drug sessions. In each group of 6, 2 were given meprobamate

(1600 mg), 2 dexamphetamine (20 mg) and 2 placebo on a double-blind basis. The meprobamate group did not differ significantly from the placebo group in its reaction time to any word category, but did respond more slowly to nontaboo words which followed taboo words than to those which came before presentation of the 1st taboo word. The dexamphetamine group reacted similarly, but did respond more slowly to taboo words. The reaction time difference between taboo and nontaboo words was also greater in the dexamphetamine group. Neither the meprobamate nor the dexamphetamine group differed from the placebo group in percentage of incorrect responses to any word category. All groups responded more slowly to and had a higher percentage of incorrect responses to taboo words than to nontaboo words, indicating the efficacy of this sort of stimulus as a useful disrupter of performance. Dexamphetamine may enhance the level of conditioned anxiety responses to the socially taboo, emotionally loaded words and thus prolonged, relatively, the reaction times to these words through response competition. Meprobamate increased the latency of onset of these same conditioned-anxiety responses, and thus left relatively unaffected reaction times to taboo words, but prolonged reaction times to the next appearing nontaboo words through the same response-competition mechanism.

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2131 McGaugh, James L., Thomson, Calvin W., Westbrook, William H., & Hudspeth, William J. A further study of learning facilitation with strychnine sulphate. *Psychopharmacologia*, 1962, 3, 352-360.

The effect of strychnine injections spaced at various intervals from a training period was observed on 120 young rats, half comprised of the S1 (Tryon maze-bright) strain and half of the S3 (Tryon maze-dull) strain. Five groups of each strain, each with 6 males and 6 females, were given i.p. 1.0 mg/kg strychnine sulfate at the following intervals: 1 group 6 minutes before each daily maze trial and the re-

aining 4 groups, respectively, 1, 15, 30 and 90 minutes after each trial. The performance of groups treated before or 15 minutes following the trial was generally superior to that of groups treated 30 or 90 minutes after the trial. The greatest variance found between strain S1 and S3 occurred when injection was 30 minutes after the trial. In addition significant to sex differences between the strains, the lowest S3 means were those of groups in which the injections were administered either before or within 15 minutes after the trials, while the lowest S1 means were those of groups injected 1, 15 or 30 minutes after trials. The significance of sub-group performance dependent on sex interactions have not been found in previous investigations using these strains. Greater attention should be given in subsequent drug studies to the possible sex differences.

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4132 Uyeda, Arthur A., & Fuster, Joaquin. The effects of amphetamine on tachistoscopic performance in the monkey. *Psychopharmacologia*, 1962, 3, 463-467.

Male rhesus monkeys trained to perform choice-responses (accuracy and reaction time) to pairs of briefly presented (10 msec) tachistoscopic visual cues received amphetamine (0.75-1.5 mg i.m.) or placebo. Animals were subjected to 50 control trials, and 1 hour after the final trial, either drug or placebo was administered. Following 10 minutes of readaptation to the ambient level of illumination, the animal was tested in another 50 trials. Each animal was given to both amphetamine and placebo treatment on 2 different days. Mean accuracy improved slightly, and a significantly shorter reaction time was observed after amphetamine injection. Similar results were previously obtained by electrostimulation of the mesencephalic reticular formation, and appear to corroborate the hypothesis of a reticulotropic action exerted by amphetamine.

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4133 Shurtleff, Donald, Mostofsky, David, & DiMascio, Alberto. The effects of some phenothiazine derivatives on the discrimination of auditory clicks. *Psychopharmacologia*, 1962, 3, 153-165.

The effects of chlorpromazine, promethazine, perphenazine and trifluoperazine on discrimination of several standard auditory pulse rate frequencies was studied in 30 normal male subjects. Four groups of 5 subjects were each administered placebo and 1 drug at 4 dose levels: chlorpromazine and promethazine each at 25, 50, 100 and 200 mg; trifluoperazine and perphenazine each at 2, 4, 8 and 16 mg. Ten subjects were used as controls. The 3-category Method of Constant Stimuli was used to estimate the subject's sensitivity to auditory pulse frequency differences. Two measures were used for discrimination; the difference limen (DL) and the standard deviation (SD) of difference judgements. At both high and low standard frequencies, chlorpromazine impaired discrimination while promethazine impaired discrimination only at the higher frequency. Increases in the DL under the higher doses of chlorpromazine was related to a systematic increase in the use of equal judgements at these dose levels. Perphenazine and trifluoperazine did not impair discrimination, however, a "crescent"-shaped dose curve for DL's was noted on perphenazine, consistent with similar dose effects reported for other behavioral measures.

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4134 Aston, Roy, Sekino, Eiji, & Greifenstein, Ferdinand E. Quantitation of drug effects upon conditioned avoidance behavior in the rat. *Toxicology and Applied Pharmacology*, 1962, 4, 393-401.

The effect of pentobarbital, chlorpromazine, propiomazine and reserpine upon conditioned avoidance behavior in rats were studied quantitatively using a modification of the technique of Cook and Weidley (1957). The depression of CAR's was found to be due both to a drug-induced indifference (reduction of anxiety or loss of fear moti-

vated behavior), and to sedation, muscular weakness and ataxia. At equipotent doses, all tranquilizers were found to possess the same degree of specific activity (reduction of anxiety, etc.), while pentobarbital showed much less specificity in this context. When the influence of acutely administered reserpine was compared to the chronically administered drug, no qualitative differences were seen as ptosis, lethargy and depression were similarly observed.

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2135 Buchel, Laïa, & Levy, Jeanne. II. - Sur les propriétés neuroleptiques du triperidol. [On the neuroleptic properties of triperidol.] *Thérapie*, 1962, 17, 1063-1084.

Catalepsy induction was studied in mice by means of injections of 0.5-5 mg/kg triperidol i.p. or s.c., and in rats by oral administration of 5-10 mg/kg. The higher doses induced catalepsy. Subsequent tests with i.p. and s.c. administration in rats indicate similar results, young rats being more sensitive to triperidol than older animals. Caramiphen and trihexyphenidyl at doses of 20 mg/kg are capable of exercising a protective action against catalepsy induced by triperidol, while diethazine is ineffective. At noncataleptic doses of 0.075-0.1 mg/kg, triperidol exercises a depressant effect on investigative activity as measured by the number of movements per 5 minutes. At noncataleptic doses, triperidol is antagonistic to dexamphetamine, in both species and for various routes of administration, both in the sense of calming hyperactivity induced by low doses of amphetamine, and in protecting the mice against the lethal effects of LD₅₀ doses of amphetamine. Triperidol is likewise antagonistic to caffeine and cocaine as measured by effects on behavior and activity patterns. At doses of 1 mg/kg and higher, it tends to reduce mouse body temperature, but less so than haloperidol. At noncataleptic doses, triperidol potentiates sleep induced by chloral hydrate or hexobarbital. The percentage of failures in the chimney-climbing test is as great with 1 mg/kg triperidol as with 4 times

the amount of haloperidol. At noncataleptic doses it inhibits apomorphine-induced chewing action, but is ineffective against electric shock, even at liminal cataleptic doses. Phenylbenzoquinone-induced convulsions are successfully controlled by noncataleptic doses.

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2136 Wolf, Harold H., Swinyard, Ewart A., & Clark, Lincoln, D. The differential effects of chlorpromazine and pentobarbital on two forms of conditioned avoidance behavior in *Peromyscus maniculatus gracilis*. *Psychopharmacologia*, 1962, 3, 438-448.

The acquisition, extinction and acute effects of chlorpromazine and pentobarbital were studied on 2 types of conditioned shock avoidance behavior: arboreal, climbing a vertical pole, and terrestrial, sitting on a nonelectrified pan located at grid level in *Peromyscus maniculatus gracilis*, a subspecies of deermouse. Two groups of 24 animals each were trained to 1 of the CAR's. The 12 animals from each group used for extinction trials were at the same level of conditioning. At the time of peak drug activity, 4 conditioned avoidance trials were given. Groups were reversed 48 hours later and reconditioned again to the above criterion. After 4 trials, the animals received chlorpromazine 2.0 and 4.0 mg/kg i.p. and pentobarbital 7.3 and 14.6 mg/kg i.p. At the end of 48 trials, the arboreal group showed a significantly higher level of conditioning than the terrestrial: (87% and 56% respectively), was more resistant to extinction and less susceptible to drug suppression. Chlorpromazine at 2.0 mg/kg significantly depressed the terrestrial response. At 4.0 mg/kg, both responses were affected, the terrestrial more markedly. Pentobarbital at both dosage levels had negligible effects on the arboreal response while it suppressed the terrestrial. The TD₅₀ was calculated for each drug by the method of Litchfield and Wilcoxon (1949).

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2137 Willett, R.A. The effect of a stimulant and a depressant drug in the serial rote learning of nonsense syllables. *Psychopharmacologia*, 1962, 3, 23-34.

Results were obtained for 73 healthy women in the serial rote learning of a list of 12 nonsense syllables. The 4 drug groups of 17 to 19 each, consisted of 2 dexamphetamine groups (10 mg), a placebo group and an amytal group (4.5 grains) were used. Drug administration followed the double-blind technique, 45 minutes prior to testing for all groups with exception of the 2nd dexamphetamine group, which was tested 90 minutes after drug administration without a blind technique. The amphetamine groups showed fewer behavior oscillations. Predictions, however, that the bowing of the serial position curve would be least for the amphetamine groups and that it would show more associative errors were not confirmed. The possibility that drug dosage and administration, particularly the need to observe the effects of cumulative dosage, were inadequate for confirmation of predictions was elucidated.

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2138 Costello, C.G. The effects of meprobamate on kinesthetic figural after-effects. *British Journal of Psychology*, 1962, 53, 7-26.

The effects of meprobamate (800 mg p.o.) on kinesthetic figural after-effects were investigated in 20 paid volunteers, aged 14-47 years, of at least average intelligence, each of whom also received a placebo. Testing with the subject blindfolded was done 1.5 hours after treatment or 2.5 hours after a light meal. Subjects compared the sizes of blocks (Eysenck 1955). Subjects tended to overestimate the test block width during prestimulation trials, a fact which was negatively correlated with extraversion measured by the MPI). Meprobamate reduced this tendency toward overestimation as well as the size of figural after-effects produced by rubbing a stimulus block wider than the test block. These results occurred only in the case of descending trials. Extra-

version was not significantly correlated with any of the measures of figural after-effect.

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2139 Stewart, Jane. Differential responses based on the physiological consequences of pharmacological agents. *Psychopharmacologia*, 1962, 3, 132-138.

Male hooded rats were trained to make differential escape responses based solely on the different physiological states brought about by chlorpromazine, imipramine, prochlorperazine, acepromazine, perphenazine and prothipendyl. The test drug, administered i.p., was never given more than twice a week, and on days between test drugs, daily trials were given under normal training conditions. Three groups of 10 animals each were used as follows: 2 groups were trained to differentiate between saline and chlorpromazine while the 3rd was trained to differentiate between saline and imipramine. When responses were well established, "test drugs" were substituted for the "training drugs" in an attempt to determine the degree of transfer of learned response from the "training drug" to the "test drug". Chlorpromazine-induced response transferred to acepromazine, perphenazine and prothipendyl, yet there was no transfer from chlorpromazine to prochlorperazine or to imipramine at the doses studied. The imipramine-trained response did not transfer to either chlorpromazine or acepromazine. The animal's behavior is guided by a particular constellation of physiological changes, i.e., changes in muscle tonus and body temperature. Thus the present study could serve as a starting point for a detailed study of the comparative effects of the more complex drugs used in this study with drugs known to have more specific and limited physiological effects.

Ayerst Research Laboratories
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Montreal, Quebec
Canada

Behavioral studies
Abstract 2140

2140 Kinnard, William J., Aceto, Mario D.G., & Buckley, Joseph P. The effects of certain psychotropic agents on the conditioned emotional response behavior of the albino rats. *Psychopharmacologia*, 1962, 3, 227-230.

Conditioned emotional response (CER) was used as a drug screening procedure in male Wistar rats. A wide dosage range was administered i.p.: chlorpromazine 0.5-3.0 mg/kg, reserpine 0.5-0.6 mg/kg and mephenoxalone 15-75 mg/kg. Dosage level was kept below that producing motor depression; chlorpromazine was administered in a motor depressant dose only when lower doses did not produce attenuation in the CER program. None of the drugs produced an attenuation in the "anxiety" response. Drug administration was repeated at intervals of 3-7 days with normal saline administered in intervals between tests. Animals initially placed in a Foringer Rat Box

(single lever and water dipper) were trained and when stabilization of lever pressing was achieved, a program using shock and pretone was used so that, finally, complete suppression developed. Attenuation of anxiety was noted by the return of some degree of lever pressing during the tone period when suppression normally occurred and degree of attenuation was a measure of potential ataractic activity. This study supports the warning (Hunt 1960) against equating the anxiety produced in the CER program to clinically observed anxiety; the technique did not give reliability in screening ataractic agents.

Department of Pharmacology
University of Pittsburgh
Pittsburgh, Pa.

See also 2003, 2051, 2104, 2192, 222

41 Kato, R., Chiesara, E., & Vassanelli, Stimulating effect of some inhibitors of drug metabolisms (SKF 525 A, Lilly 18947, Lilly 32391 and MG 3062) on excretion of ascorbic acid and drug metabolisms. *Medicina Experimentalis*, 1962, 6, 4-260.

Studies were made on the stimulating effect of drug inhibitors on drug metabolism and ascorbic acid biosynthesis in female rats (prague-Dawley and Long-Evans). The determination of hexobarbital, strychnine and meprobamate metabolism was carried out *in vitro* by incubation of liver slices or liver microsomal fractions. In some experiments, *in vivo* catabolism of meprobamate measured after i.p. injection of 10 mg/kg of meprobamate was carried out. SKF 525 A, Lilly 18947, Lilly 32391 and MG 3062 (all inhibitors) were administered at 50 mg/kg 48 hours before the termination of drug metabolism. For termination of urinary ascorbic acid and hexobarbital, inhibitors were given 10 mg/kg i.p. b.i.d. for 4 days. Stimulation of ascorbic acid synthesis and of hexobarbital, strychnine and meprobamate catabolism was observed in the pretreated rats. The inhibitors could therefore be considered to have facilitating effects on the microsomal drug catabolizing enzymes as well as inhibiting ascorbic acid synthesis, which is also a property of drugs they inhibit such as phenobarbital, phenacyclodol and glutethimide.

Institute of Pharmacology
University of Milan
Milan, Italy

42 Ford, Donald H., & Wolfson, Sonia. The effect of reserpine on the utilization of ^{131}I -labelled triiodothyronine by the CNS of the male rat. *Acta Neurologica Scandinavica*, 1962, 38, 159-165.

Male reserpinized (30 $\mu\text{g}/100\text{ g/day}$ i.p. for 2-3 weeks) rats received an intramuscular injection of 0.5 $\mu\text{g}/\text{kg}$ ^{131}I -labeled triiodothyronine (T3). The T3 activity was 15.50-27.4 $\mu\text{g}/\text{kg}$. The animals were killed at half, 1, 2, 4 or 7 hours after injection with labeled hormones. Blood samples were taken 1 minute after T3 injection and at the

termination of the experimental period. Ascending paper chromatographic analysis showed that a mean of 75.2% radioactivity was associated with the T3 carrier spot; the remainder was associated mainly with iodide and mono- and diiodotyrosine. While the rats received enough reserpine to be "tranquilized", this dosage had no effect on the uptake and degradation of labeled-triiodothyronine by the nervous system, muscle or anterior pituitary lobe. Furthermore there was no indication that reserpine in any way interfered with iodide concentration by the thyroid subsequent to deiodination of T3 by other tissues in the intact animal.

Department of Anatomy
450 Carson Ave.
Brooklyn 3, N.Y.

2143 Kaumann, A.J., Coussio, J.D., & Izquierdo, J.A. Der Einfluss von Imipramin auf die Blutdruck- und Ekg-Wirkungen von Adrenalin, Noradrenalin, Hydroxytryptamin und Hypertensin. [The influence of imipramine on blood pressure and ECG activity by epinephrine (adrenalin), levarterenol (noradrenalin), hydroxytryptamine and angiotensin.] *Medicina Experimentalis*, 1962, 6, 1-13.

The influence of imipramine on the pressor and ECG responses to epinephrine, levarterenol, 5HT and angiotensin was studied in 20 pentobarbital narcotized dogs. In 4 dogs pretreated with reserpine 48 hours previously, the effects of imipramine, epinephrine and levarterenol were studied. The dosages employed were: 0.5-2.0 $\mu\text{mg}/\text{kg}$ levarterenol monohydrate-ditartrate, 1.0-2.0 $\mu\text{mg}/\text{kg}$ epinephrine chlorhydrate, 20.0 $\mu\text{g}/\text{kg}$ serotonin creatinine sulfate, 0.2 $\mu\text{g}/\text{kg}$ angiotensin, 5.0-10.0 mg/kg azamethonium (ganglionic blocking agent), 3.0 mg/kg imipramine and 250 $\mu\text{mg}/\text{kg}$ reserpine. Imipramine stimulates the heart rate and moderately influences cardiac repolarization. Epinephrine after imipramine causes variable hyperpressure responses while the ECG remains unaffected. Levarterenol after imipramine elicits a marked blood pressure rise and tachycardia with significant changes in repolarization. The pressure effects of 5HT and angiotensin are accentuated after imipramine, while no change in the

ECG was detected. In reserpinized dogs, imipramine abolishes hypotension, restoring normal tension and exerting moderate influence on cardiac repolarization. The potentiation of levarterenol hypertension after reserpine is still more accentuated after imipramine, leading to tachycardia and repolarization changes. Azamethonium only slightly influenced the effects of the other agents.

Cátedra de Farmacología Experimental
Facultad de Farmacia y Bioquímica
Buenos Aires, Argentina

2144 Anderson, Elvin L., Bellinzona, G.B. Craig, Paul N., Jaffe, Gerald E., Janeway, Katherine P., Kaiser, Carl, Lester, Bruce M., Nikawitz, Edward J., Pavloff, Alex M., Reiff, Harry E., & Zirkle, Charles L. Synthesis of phenothiazines. *Arzneimittel-Forschung*, 1962, 12, 937-941.

Pharmacological and clinical data has shown that substitution of the 4-methylpiperazine group for the dimethylamino group in 10-(3-aminopropyl)-phenothiazine derivatives results in compounds with enhanced tranquilizing and antiemetic activities. Therefore, substituted piperazine derivatives of 2-chloro- and 2-trifluoromethyl-phenothiazines were synthesized and studied. Most of the compounds (42), 4-substituted-piperazinylalkyl derivatives, are listed in tabular form, replete with physical and analytical data. Pharmacological data on thiopropazate and fluphenazine is reviewed. Complete data on all procedures required for organic synthesis is included.

Research and Development Division
Smith Kline and French Laboratories
Philadelphia, Pa.

2145 Perényi, L., Csötrötök, L., Demeter, Magda, & Földes, I. Anwendung von Ionaustauscher-Chromatographie zur spektrofluorometrischen Bestimmung des Serotonins. [Use of ion-exchange chromatography for the spectrofluorometric determinations of serotonin.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 12-13. [Abstract]

Following a critique of the method of Udenfriend et al. for the chemical determination of 5HT, the authors suggest the use of ion-exchange chromatography for the isolation of 5HT, replacing the usual extraction by organic solvents. The spectrofluorometric method which permits the determination of 0.1 μ g of 5HT is described.

Korányi State Tuberculosis Institute
Budapest, Hungary

2146 Forney, Robert B., Hughes, Francis W., Hulpieu, Harold R., & Clark, William C. Rapid early metabolism of ethanol in the mouse. *Toxicology and Applied Pharmacology*, 1962, 4, 253-256.

Male Harlan mice were given 4 g/kg ethanol administered i.p. as a 20% solution. Immediately after injection each individual mouse was placed in a Waring Blender supported on a wire platform above the diluent. At intervals of 0, 0.5, 1, 2, 3 and 4 hours the mouse was dropped into the diluent and homogenized. The entire homogenate was immediately steam distilled and analyzed for ethanol. Ethanol was found to disappear rapidly during the 1st 30 minutes and thereafter at a slower, almost constant rate.

Department of Pharmacology and Toxicology
Indiana University School of Medicine
Indianapolis, Ind.

2147 McColl, J.D., & Rice, W.B. Antagonism of tremorine by benactyzine and dioxolane analogs. *Toxicology and Applied Pharmacology*, 1962, 4, 263-268.

The antagonism of tremorine convulsions (ED₅₀ 5.8 mg/kg) in CFW mice was investigated using trihexyphenidyl (17.8 mg per kg), chlorpromazine (17.8), diethazine (17.8), meprobamate (10.0 and 100.0), benactyzine (10.0), chlorphenoxamine (10.0), nonylmethyldioxolane (10.0), dioxamate (10.0), promoxolane (10.0) and promoxolane carbamate (10.0). Additionally the last 4 compounds were used with benactyzine and the combination of chlorphenoxamine with nonylmethyldioxolane was used.

marked potentiation of antagonistic effect as observed with benactyzine and dioxolane analogues (promoxolane and dioxamate).

Research Laboratories
Frank W. Horner Limited
Montreal, Quebec
Canada

2148 Frommel, E., Fleury, C., von Ledebur, I., & Beguin, M. Concerning the action of electroshock on the cortical and subcortical levels. An experimental investigation. *Medicina Experimentalis*, 1962, 6, 173-176.

lingual and occipital electrodes were used for the production of electrocrisis in guinea pigs. The threshold voltage is established on the previous day and then, in experimental animals, an excess voltage of 50% is applied to animals previously injected s.c. with 5 mg/kg amphetamine. Electroshock produces a refractory phase toward amphetamine-induced psychomotor agitation, and this lasts ca. 30 minutes. However repeated electroshock crises do not affect the action of amphetamine if the latter is injected after the end of this refractory phase. Electroshock cortical and subcortical inhibition is of very brief duration and is reversible.

Institute of Experimental Therapeutics
Geneva University School of Medicine
Geneva, Switzerland

2149 Shagass, Charles, Bittle, Robert M., Masling, Hugh H., & Schwartz, Marvin. "Barbiturate thresholds" in the rabbit. *Psychopharmacologia*, 1962, 3, 204-211.

Thiopental (1 and 2 mg/kg/30 seconds, injection rate) was used for barbiturate threshold determination in rabbits. Two methods of assay were used: head drop, indicating complete loss of tone in the neck muscles, and conflict experiments (anticipation of pain on feedings, i.e., electroshock 6-8 minutes after the start of a 1-minute feeding period). Intravenous injections of 5 mg amphetamine were given 15 minutes before and 1 mg/kg chlorpromazine 30 minutes before the thiopental

test to some animals. Others were given 10 U ACTH i.v. about 8 hours before the test. The 1st 2 groups were selected for anticipated antagonistic and synergistic effects in relation to thiopental. ACTH was tried for possible protective effect. Negative results were obtained in relation to experimental conflict, which appear due mainly to the predominant effect of restrictive feeding in reducing the threshold. In all tests amphetamine and ACTH produced no consistent effects while chlorpromazine caused a marked decrease in the threshold. Rabbit barbiturate thresholds seem to resemble those in man.

Department of Psychiatry
College of Medicine
State University of Iowa
Iowa City, Iowa

2150 Glow, Peter H. The antagonism of methyl phenidate and iproniazid to bulbo-capnine catatonia in the rat. *Australian Journal of Experimental Biology and Medical Science*, 1962, 40, 499-504.

The effects of methylphenidate on spontaneous psychomotor activity (method of Dicker et al. 1957) on bulbo-capnine-treated male hooded inbred rats were studied. Fifty mg/kg bulbo-capnine produces a complete cessation of movement. Depending on the dose strength of methylphenidate, there is a stepwise corresponding increase in the amount of spontaneous psychomotor movement. The effect of this dosage of bulbo-capnine (50 mg/kg) is almost indistinguishable from those effects reported with 5 mg/kg reserpine. Methylphenidate (20-60 mg/kg) has some potency as an antagonist to the catatonicleike action of bulbo-capnine, but iproniazid (25-100 mg/kg) was ineffective.

Department of Psychology
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Adelaide, Australia

2151 Russell, R.L., & Westfall, B.A. Alleviation of barbiturate depression by fat emulsion. *Anesthesia and Analgesia*, 1962, 41, 582-585.

Lipomul (a 15% cottonseed oil emulsion, 1.5 g fat/kg) was infused i.v. into 10 male rats immediately following thiopental (20 mg/kg i.v.) administration, and 11 male rats which acted as controls received fat free Lipomul to compare the effect on duration of anesthesia. A 10% corn oil emulsion was administered to 10 male rats and 10 controls to determine the effect of corn oil emulsion on duration of thiopental anesthesia. Thiopental (30-100 mg per 100 ml) in buffered saline was added to brain slices pretreated with corn oil emulsion in order to measure the effects of the emulsion on oxygen consumption. In in vivo experiments with cottonseed oil emulsion, the mean duration of anesthesia for the control group was 13.6 minutes, while that for animals receiving emulsified cottonseed oil was 9.4 minutes. In animals receiving corn oil emulsion, mean duration of anesthesia was 8.1 minutes, while that for controls was 11.6 minutes. Differences in duration of anesthesia were statistically significant. In vitro, a thiopental concentration of 30 mg per 100 ml resulted in no change in oxygen consumption as compared with controls. However, a concentration of 100 mg/100 ml did depress the QO_2 significantly at the 60 and 90 minute intervals. The emulsion alone apparently acted as a stimulant to O_2 uptake by brain slices. The duration of thiopental anesthesia was decreased significantly in rats by an infusion of cottonseed oil and corn oil emulsions. The increased QO_2 of brain slices in the presence of corn oil emulsion is probably due primarily to the emulsifying agent, as neither corn oil nor a 5% glucose solution altered O_2 uptake in the absence of thiopental.

Department of Physiology and Pharmacology
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Columbia, Miss.

2152 Echlin, Francis A., & Battista, Arthur. Regional differences in the epileptiform electrical response of the unanesthetized cerebral cortex to acetylcholine. *Neurology*, 1962, 12, 551-559.

In 20 monkeys electrocorticograms were

made of changes in the resting electrical activity of the brain following the topical application to the cortical surface of acetylcholine or eserine. Concentrations were acetylcholine 0.2-10% and eserine 0.2%. There were marked regional differences in the epileptiform electrical response of the monkey cerebral cortex to acetylcholine. The occipital and posterior parietal cortex was much more sensitive to this form of stimulation than other cortical areas. Any cortical area is capable of responding with the wrong rhythmic epileptiform electrical discharge to an adequate stimulus, but the cortical area from which such firing may be most easily precipitated varies with the nature of the stimulus (electric or acetylcholine). Stimulation of an area of cerebral cortex with acetylcholine causes a widespread lulling of the threshold to acetylcholine stimulation of other areas throughout the cortex. The responsible mechanism is presumably mediated through projections to the brain stem or thalamic reticular areas. In relation to motor, premotor and anterior temporal cortex, the mechanism is more highly developed than in other regions, i.e., a mechanism which inhibits the effect of topical acetylcholine stimulation and prevents its tendency to produce synchronization, high-voltage rhythmic discharge and epileptiform seizures. Chronic partial denervation of an area in the cortex eliminates the inhibitor mechanism thus rendering an area of the cortex equally susceptible to topical acetylcholine stimulation.

Department of Neurology
Lenox Hill Hospital
New York, N. Y.

2153 Ursin, Holger. The lack of effect of LSD 25 on amygdaloid and cortical attention responses. *Psychopharmacologia*, 1962, 3, 317-330.

The behavioral attention response (behavioral arousal associated with contralateral searching movements) was induced in cats by stimulation of the temporal lobe neocortex, the amygdaloid nuclear complex and the mesencephalic reticular formation. The threshold of the attention responses was tested before and after i.v. or i.p. injection of LSD (5-200 μ g/kg, but usually 10-50 μ g/kg).

The threshold was found to be unaltered by the drug for all CNS structures studied. General behavioral changes and "attention response" thresholds (opening of the eyes, retraction of the nictitating membrane, arrest of ongoing activity, pupillary dilation, etc.) were used in evaluation. Since there was no effect of LSD on the telencephalically-induced attention response while chlorpromazine has a clear blocking effect under the same circumstances, these 2 psychotropic drugs apparently have no simple opposing effect on nervous system function. The results are believed to have some bearing upon the possibility that the main effect of LSD is due to interference with sensory inflow to the CNS.

Neurophysiological Laboratory
Anatomical Institute
University of Oslo
Oslo, Norway

2154 Gray, J. E., McWade, D. H., Johnston, L. L., Larson, E. J., & Freyburger, W. A. Toxicopathologic studies of α -methyl- and α -ethyltryptamine acetates (Monase). I. Acute, subacute, and miscellaneous studies. *Toxicology and Applied Pharmacology*, 1962, 5, 547-560.

Acute toxicity determinations on α -methyltryptamine and etryptamine (α -ethyltryptamine acetate) were made in Swiss mice following i.p. administration and in Upjohn Sprague-Dawley rats given the drugs orally after a 24-hour period of starvation. Subacute oral toxicities were also worked out in rats and Beagle dogs. In 28-day rat studies, α -methyltryptamine and etryptamine were well tolerated at 3 and 10 mg/kg. At higher doses increasing retardation of body weight gains and signs of CNS stimulation occurred. No drug-related alterations in dogs which received doses of 1, 3 and 10 mg/kg of α -methyltryptamine were noted, though 1 dog lost a significant amount of weight during the month study. Dogs which received 30 mg/kg became acutely intoxicated but rapidly developed tolerance during a week of drug dosage. Daily doses of 3, 10, and 30 mg/kg etryptamine produced no clinical or histologic evidence of side effects in dogs during the 28-day period. After 90 mg/kg, 3 dogs showed signs of CNS stimu-

lation and the livers of 2 of these were severely congested. Etryptamine was appreciably better tolerated than α -methyltryptamine. Further doses of etryptamine which were well tolerated orally by rats and dogs during subacute studies were 30-50-fold greater than the anticipated human therapeutic dose. Etryptamine appeared to be without significant cardiovascular toxicity in the dog. In rabbits, muscle irritation was essentially nil at 1 mg/kg and moderate at 10 mg/kg. Also daily p.o. doses of 10 mg/kg produced no effect on rat reproduction.

Research Laboratories
The Upjohn Company
Kalamazoo, Mich.

2155 Kato, R., Vassanelli, P., Frontino, G., & Bolego, A. Metabolism and distribution of carisoprodol in tissues and organs of the rats. *Medicina Experimentalis*, 1962, 6, 149-157.

The metabolism and tissue distribution of carisoprodol (150-200 mg/kg i.p.) was studied in female Sprague-Dawley rats. Assay was by the method of Hoffman and Ludwig and animals were sacrificed at various intervals after drug administration. The concentration of carisoprodol reached a maximum 20-30 minutes after injection with marked accumulation occurring in liver and kidney and little in muscle or brain tissue. Only 7.5% of injected carisoprodol was eliminated during 48 hours after administration, while 5.5% was eliminated within 12 hours postinjection. Within 5 hours after drug administration, carisoprodol concentration fell to 20% of that observed after 30 minutes. There was a low rate of excretion of the drug in either urine or feces. The biological half-life was about 3 hours. SKF 525 (25 mg/kg i.p.) inhibited carisoprodol metabolism in vivo and prolonged the duration of paralysis in these animals. In vitro experiments suggested that a liver microsomal enzyme (which required TPNH and oxygen) was largely responsible for the metabolism of carisoprodol.

Institute of Pharmacology
University of Milan
Milan, Italy

2156 Cahen, Raymond, Montagne, Jacqueline, Pessonnier, Jeanne, & Pessonnier, André. Etude pharmacologique de la 2-diéthylaminopropiophénone. I. Toxicité. [A pharmacological study of 2-diethylaminopropiophenone. I. Toxicity.] *Thérapie*, 1962, 17, 373-412.

A comparative study of the acute, subacute and chronic toxicity of 2-diethylaminopropiophenone and its closely related analogue dexamphetamine in mice and rats showed that the lethal doses are 1.33-1.6 times as high for the new derivative as for dexamphetamine in mice and 2.13-2.8 times as high in rats (i.p. and p.o.). Addition of highly polymerized polyhydroxyethylenehydroxypropylene (M.W. = 8250) to provide sustained release had no apparent effect on toxicity, and long-term administration of the mixture to rats for 146 days (at levels up to 0.01% of the diet or 5% of the LD₅₀) produced no significant ill effects, only a slight inhibition of growth being seen at the highest dosage.

Centre de Recherches Lafon
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2157 Benesová, O., Bohdanecký, Z., & Votava, Z. Electrophysiological comparison of the action of imipramine and propazepine. *Psychopharmacologia*, 1962, 3, 423-431.

Imipramine and its structural isomer propazepine were compared using 3 electrophysiological methods: bioelectrical activity of cortical and subcortical areas in rabbits with implanted electrodes, changes in the motor thresholds in rabbits with permanent epidural electrodes and self-stimulation in rats (Olds 1954, 1960). EEG records in cortical and subcortical areas (hippocampus, thalamus) in rabbits with implanted electrodes after the administration of both drugs (5 mg/kg i.v.) did not differ. Imipramine had a greater antagonistic effect to cortical desynchronization and subcortical synchronization evoked by physostigmine (0.1 mg/kg i.v.). The potentiation of thiopental anesthesia measured by motor threshold in rabbits with permanent epidural electrodes was greater after the administration of propazepine (2.5 mg/kg i.v.). Imipramine (1, 1.5 and 2 mg/kg i.p.)

decreased the rate of self-stimulation in rats with electrodes implanted in ventro-lateral hypothalamus, while propazepine 1.5 mg/kg i.p. caused a significant increase in the rate of self-stimulation the 2nd day and at 2 mg/kg i.p. a significant decrease on the 1st day after administration. Clinically an increased positive motivation could have some importance in relation to the expected use of propazepine as an antidepressant in accord with Stein's hypothesis (1962), that "a depressed patient suffers from insufficient positive reinforcement (reward)."

Department of Pharmacology
Medical College of Hygiene and Research
Prague, Czechoslovakia

2158 Kerley, T. Lamar, Newberne, James W., Brinkman, David C. The acute and chronic toxicities of chlorphenoxamine. *Toxicology and Applied Pharmacology*, 1962, 4, 638-649.

In male Swiss-Webster mice, the CD₅₀ for chlorphenoxamine by the intragastric route was 315 mg/kg and the LD₅₀ 575 mg/kg. Parallel studies with phenoxethamine showed its CD₅₀ to be 470 mg/kg and the LD₅₀ to be 650 mg/kg when given intragastrically. Both drugs produced tonic-clonic convulsions and death from respiratory failure. The i.v. LD₅₀ of chlorphenoxamine in dogs was 30.8 mg/kg. Higher doses were associated with apprehensiveness and convulsions; the convulsive state could be easily controlled by small i.v. doses of pentobarbital. A chronic 26-week toxicity study in rats (112.8 mg/kg/day), and chronic toxicity in dogs (30 mg/kg/day for 13 weeks and also for 29 weeks) was undertaken. Chlorphenoxamine in rats did not produce significant pathological alterations or alteration in the growth rate. Chlorphenoxamine was given to dogs for 18 weeks at 10 mg/kg/day then for an additional 29 weeks at 30 mg/kg/day; it initially caused a mild emetic response in some dogs and loss of body weight was apparent. Otherwise the drug was well tolerated for the experimental period. No histologic or hematologic abnormalities were noted due to the drug.

Research Center
Pitman-Moore Company
Division of The Dow Chemical Company
Indianapolis, Ind.

2159 Petöcz, Lujza, & Komlós, E. Über die Zusammenhänge zwischen den i.v. Toxizitätswerten und der Einspritzungsgeschwindigkeit. [Relationships between the i.v. toxicity and the rate of injection.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 47-48. [Abstract]

Changes in the i.v. LD₅₀ of 15 different substances were determined in mice in relation to the rate of administration of the solution (0.01 ml/g at varying concentrations). The results show that these substances can be divided into 3 groups on the basis of the effect of the rate of injection: one group (opiate alkaloids, Frenolon, sodium iodipamide) in which the rate of injection had no effect on LD₅₀, a second group (perphenazine, imipramine, Urokon, pentetrazol) in which the LD₅₀ was increased about 50% by a decrease in injection speed, and a third group in which the LD₅₀ was doubled or more by a decrease in the rate of injection; the latter group could be subdivided into those drugs (benzonate, N 640, N 685, Gastropin) showing a linear relationship between LD₅₀ and injection speed and those drugs (chlorpromazine, promazine, Doryl, ephedrine) showing an exponential relationship. These differences cannot be explained on the basis of the chemical or pharmacological properties.

Laboratory of Pharmacology
United Drug and Food Industries
Budapest, Hungary

2160 Kelentey, B., & Pusztai, F. Die Serotoninwirkung auf den Liquordruck. [Effect of serotonin on spinal fluid pressure.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 26. [Abstract]

The effect of 10, 50 and 100 µg/kg 5HT, i.v., on the spinal fluid pressure, blood pressure, respiration and intestinal activity was studied in chloralosed cats. Depending on the dosage, 5HT increased the blood

pressure, spinal fluid pressure, intestinal tone and respiratory volume. The increase in spinal fluid pressure always appeared later than that in blood pressure, but the effect lasted a relatively long time [30-45 minutes]. At the point of maximal spinal fluid pressure, the rate and amplitude of the spinal fluid pulse reached a minimum, indicating a disturbance in cerebral circulation. This increase in spinal fluid pressure did not occur after i.v. reserpine. The increase in spinal fluid pressure produced by serotonin could be counteracted by LSD, the specific antagonist, but could not be prevented by antihistamines, sympatholytic agents or anticoagulants. No 5HT could be detected in the brain or spinal fluid, even after i.v. injection of a large dose (1, 2 or 3 mg/kg), indicating that it is unable to pass the blood-brain-spinal fluid barrier.

Institute of Pharmacology
Medical University of Debrecen
Debrecen, Hungary

2161 Ferguson, Hugh C. Dilution of dose and acute oral toxicity. *Toxicology and Applied Pharmacology*, 1962, 4, 759-762.

Doses of 12 compounds (amphetamine, benactyzine, diphenhydramine, mephenesin, pentobarbital, pentetrazol, phenylbutazone, potassium cyanide, etc.) were administered by stomach tube to groups of fasted Sprague-Dawley rats in volumes corresponding to 5, 2.5 and 1.25% body weight. The number of dead animals was recorded after 24 hours. These compounds were also administered to Swiss-Webster mice given in the water 4 hours before drug administration. Further LD₅₀'s for pentobarbital, potassium cyanide, procaine and sodium fluoride were established in mice at 5 and 1% body weight levels. Results show the same trend for all 12 compounds; the greater the dilution of the toxic dose, the greater the death rate. Dilution may alter not only toxicity, but also many other pharmacological responses and determinations.

Distillation Products Industries
Division of Eastman Kodak Company
Rochester 3, N. Y.

2162 Morillo, Arturo, Revzin, Alvin M., & Knauss, Thomas. Physiological mechanisms of action of chlordiazepoxide in cats. *Psychopharmacologia*, 1962, 3, 386-394.

Acute and chronic experiments were performed on 18 cats in order to investigate the action of chlordiazepoxide. With electrodes stimulating the lateral nucleus of the amygdala and recording from the basal hippocampus, the magnitude and time course of the produced changes upon the electrical and behavioral responses were studied. The effects upon the diffuse thalamocortical system were also investigated by stimulating the nucleus centralis lateralis of the thalamus and recording the recruiting response from the pial surface of the suprasylvian gyrus. For acute experiments, chlordiazepoxide was used in single i.v. doses of 2, 5 and 10 mg/kg; in chronic study single i.m. doses of 10 mg/kg were given. In the chronic preparations, chlordiazepoxide showed a strong depressant action on the hippocampal response and a delayed "slow motion" response to stimulation of the amygdala. The diffuse thalamocortical system was unaffected. Results are interpreted as indicating a site of drug action chiefly at the amygdalohippocampal level.

Thudichum Psychiatric Research Laboratory
Galesburg State Research Hospital
Galesburg, Ill.

2163 Hansson, Eskil, & Steinwall, Oskar. Abnormal blood-brain passage of a quaternary phenothiazine derivative (S^{35} -labelled Aprobit) induced by chemical agents. *Acta Physiologica Scandinavica*, 1962, 54, 339-345.

Abnormal blood-brain passage of S^{35} -labeled Aprobit (aphenothiazine derivative) was induced by regional brief perfusion of Hg^{++} , cyanine dye 863 or unlabeled Aprobit through rabbit cerebral vessels. The test substance, radiochemically pure S^{35} -Aprobit was injected into the left cardiac ventricle after ligation of the thoracic aorta in order to augment cranial concentration in doses of 90-150 μ c/kg body weight. Cerebral uptake of S^{35} -Aprobit was recorded by means of autoradiography and radioassay.

In 2 control experiments with intact brains, almost no radioactivity was found in the brain. The results were discussed with reference to the hypothesis that blood-brain directed transport mechanisms are involved in blood-brain barring of certain groups of organic ions, specifically barring the cation Aprobit.

Department of Pharmacology
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Stockholm, Sweden

2164 Lapin, I. P. Qualitative and quantitative relationships between the effects of imipramine and chlorpromazine on amphetamine group toxicity. *Psychopharmacologia*, 1962, 3, 413-422.

Various doses of imipramine with chlorpromazine were administered to groups of 10 mice (500 in total) s.c. 30 minutes prior to administration of 20 mg/kg amphetamine and their effects compared with groups which received only amphetamine. Imipramine in small doses (0.5 - 1 mg/kg) intensified, but in large doses (60 - 100 mg) reduced the toxic effects of amphetamine motor excitation, aggressivity and lethality. The difference in influence of low and high doses suggests that dual (positive and negative) imipramine action on adrenergic synapses, previously observed in peripheral synapses, also occurs in the brain. Chlorpromazine, like imipramine, decreased (in doses of 2.5 and 5.0 mg/kg) and also increased (in doses of 0.005-0.01 mg/kg) amphetamine group toxicity. The similarity of both the tranquilizing and analeptic effect of imipramine and chlorpromazine suggest both a common mediator nature and possible localization of action. "Amphetamine group toxicity" may be applied as a sensitive test for evaluation of psychoanaleptic drug activity. With depressed patients, decrease towards the analeptic zone of action, not increase in imipramine dosage, may be proper therapeutically.

Laboratory of Psychopharmacology
Bechterev Psychoneurological Institute
Leningrad C-19, USSR

2165 Ninomiya, H., Greisman, S. E.

Buxton, R. W., & Michaelis, M. Brain enzyme changes in drug shock in the rat. *Acta Neurologica Scandinavica*, 1962, 38, 83.

Noble-Collip drum shock results in a decrease of several rat brain dehydrogenases and deaminases, an increase in glycolysis and depression of the Pasteur effect. Protein content of homogenates and mitochondria is affected by shock, and the distribution of lactic dehydrogenase between mitochondria and cytoplasm is altered. Alterations also occur in metabolite concentrations, as well as the ratio of oxidized to reduced forms of dehydrogenases. Administration of a tranquilizer [unspecified] before the shock procedure frequently eliminates these effects. Inhibition of brain cholinesterase with physostigmine increases mortality from shock, whereas inhibition of serum cholinesterase with di-isopropyl fluorophosphate does not increase mortality. Blockade of the reticuloendothelial system produces increased mortality from shock which is not a consequence of serum cholinesterase inhibition. Cerebral enzymatic activities are obviously very significant in shock.

Division of Experimental Surgery
University of Maryland School of Medicine
Baltimore, Md.

2166 Chapman, J. E., & Walaszek, E. J. Antagonism of some toxic effects of dextropropoxyphene by nalorphine. *Toxicology and Applied Pharmacology*, 1962, 4, 752-758.

Female rats received dextropropoxyphene (10-160 mg/kg i.p.) alone, or in combination with nalorphine (0.5 mg/kg s.c.) administered concomitantly with the initial convulsive episode or 10 minutes before injection of dextropropoxyphene to determine the i.p. LD₅₀, toxic effects and effects of nalorphine on dextropropoxyphene. All animals were observed for the onset and duration of salivation, depression, convulsions, rigidity, Straub tail effect and death. With doses of dextropropoxyphene greater than 30 mg/kg toxic symptoms were observed within 5-10 minutes. Site of origin for convulsions was determined by administering dextropropoxyphene to rats with spinal cords sectioned at C6. The i.p. LD₅₀ was 68 mg/kg for dextropropoxyphene-treated animals. Doses

greater than 40 mg/kg produced a short asymptomatic lag period (5-10 minutes), which preceded tonic, clonic convulsions and the Straub tail effect. Dosages in excess of 80 mg/kg produced brief convulsions which rapidly terminated in death. Nalorphine (0.5 mg/kg s.c.) injected 10 minutes before dextropropoxyphene increased the LD₅₀ to 105 mg/kg. Whereas animals not treated with nalorphine died during the initial part of the convulsant period, the nalorphine-treated animals survived with a proportionally longer convulsant period. Three groups of 8 animals received dextropropoxyphene (65 mg/kg i.p.) followed by nalorphine (0.1-20 mg/kg s.c.) administered at the initial convulsion to determine whether or not nalorphine could antagonize established convulsions. Convulsant time was diminished to 52% of controls with 0.1 mg/kg, to 39.9% with 0.5 mg/kg and to 10.2% with 20 mg/kg. Generalized convulsions were shown to be cerebral in origin.

Department of Pharmacology
University of Kansas Medical Center
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2167 Miller, Lowell D. The distribution, metabolism, and excretion of phenylamidol in the dog. *Toxicology and Applied Pharmacology*, 1962, 4, 190-199.

Phenylamidol determinations were made on samples of dog urine, blood plasma and tissue at various times after the administration of 150 or 200 mg/kg phenylamidol. Paper chromatography and spectrophotometric analyses of the urine extract before and after β -glucuronidase hydrolysis substantiated the presence of phenylamidol glucuronide as a major metabolite. In anesthetized dogs, the circulating phenylamidol disappeared rapidly from the blood stream so that within 5 minutes after injection most of the drug had been removed. Two elimination pathways were noted: one via the bile and the other in the urine. The rate of urinary excretion was 10-15% of a daily oral dose. Less than 1.5% of the administered dose was present in the urine in unmetabolized form and most of this appeared within the 1st 24-hour period. After i.v. (25 mg/kg) or oral administration, most of the drug was retained by the muscle

mass whence it was slowly released back into circulation for conjugation with glucuronic acid by the liver. Skeletal muscle appears to act as a repository for the administered drug.

Research Laboratories
Irwin, Neisler and Co.
Decatur, Ill.

2168 Erdmann, G., & Kütz, J. Experimentelle Krämpfe durch INH und ihre therapeutische Beeinflussung, auch im Hinblick auf INH-bedingte Veränderungen des EEG bei Kindern. [Experimentally induced convulsions with isoniazid (INH) and their treatment, with special reference to INH-related changes in the EEG of children.] *Monatsschrift für Kinderheilkunde*, 1962, 110, 123-125.

Oral doses of 200 mg/kg isoniazid induced convulsions in mice, and led to death within 1-2 hours. Doses of 50 mg/kg phenobarbital and 5-(2-butenyl)-5-ethylbarbituric acid (Kalypnon) successfully combated the convulsant effects of isoniazid, but as the dosage of phenobarbital was increased, the mice died despite suppression of the convulsions. Guayacolglycerineether in doses of 200 mg/kg suppresses INH-convulsions, and will prevent subsequent death. In view of the effect of isoniazid on mice, EEG's were obtained from 17 children receiving 10 mg/kg/day isoniazid for 3 days. Of the 17, 6 showed signs of hyperventilation, including 2 cases of neurological or psychic disorders, and 2 cases of suspected cerebral attacks. Suspension of INH treatment or dosage reduction is recommended in cases where EEG's reveal latent convulsive tendencies.

Universitäts Kinderklinik
Mainz, Germany

2169 Carlsson, Arvid, & Lindqvist, Margit. In vivo decarboxylation of α -methyl-dopa and α -methyl metatyrosine. *Acta Physiologica Scandinavica*, 1962, 54, 87-94.

α -Methyl DOPA and α -methyl metatyrosine were administered to mice (400 mg/kg i.p.). α -Methyl DOPA was also administered to

rabbits (200 mg/kg i.v.). At varying intervals after injection, brains were assayed for monoamines (5HT, levarterenol, dopamine and α -methyl analogues). A transient decrease in 5HT and dopamine, and a prolonged and more marked decrease in levarterenol were observed. The α -methyl amino acids underwent decarboxylation and subsequent β -hydroxylation in vivo. The drop in levarterenol and dopamine levels in brain tissue caused by the α -methyl amino acids appears largely due to displacement by decarboxylation products which may possibly also take over the functions of the physiological amines. These results suggest that α -methylated analogues of physiological amino acids may represent useful tools in the study of the formation, storage, release, degradation and physiological role of biogenic amines.

Department of Pharmacology
University of Göteborg
Göteborg, Sweden

2170 Booker, Walter M., Fisher, Edward Coffey, William, Linares, Rafael, & Bryant Jeanette. Studies on the secretion of catecholamines during carotid sinus reflex involvement. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 336-345.

Blood pressure elevation and catecholamine release during carotid clamping were studied in intact and adrenalectomized dogs under the influence of the following agents: reserpine (0.1 mg/kg i.m.) administered 3 days before the experiment, bretylium (1 mg/kg i.v.) injected just before determining the carotid sinus reflex, P-286, an alkyl urea, 2.5 mg/kg i.v. administered 2-3 times at 15 minute intervals before testing the reflex, acetylcholine (2.5 mg/kg i.v.) given every 5 minutes to deplete catecholamine levels and JB 516 (5 mg/kg i.v.) administered directly before testing the carotid sinus reflex. Booker's (1959) isolated heart method of assaying catecholamines was used. Blood pressure elevation and catecholamine release occurred in both intact and adrenalectomized animals, although both responses were markedly lessened in the latter. Traction on the sinus nerves in intact and adrenalectomized animals re-

ulted in decreased blood pressure and cessation of catecholamine release. During carotid clamping, reserpine completely blocked blood pressure response and catecholamine secretion. P-286 blocked catecholamine release and markedly reduced, but did not completely block blood pressure elevation. Bretylium, an inhibitor of postganglionic fiber activity, markedly attenuated but did not block blood pressure response of catecholamine release. The brain apparently releases levarterenol during bilateral carotid clamping.

Department of Pharmacology
Howard University Medical School
Washington, D. C.

2171 Keller, J. G., Viguera, C., & Kundzins, V. Studies on the toxicology of α -methyl- and α -ethyltryptamine acetates (Monase). I. Chronic studies. Toxicology and Applied Pharmacology, 1962, 4, 697-709.

Two MAO inhibitors, α -methyl- and α -ethyltryptamine acetate (MT and ET) were administered p.o. to 3 groups of 20 Charles River, Sprague-Dawley rats for 1 year and to 3 groups of 4 Beagle hounds for 6 months. Rats received 3.0, 10 or 30 mg/kg/day. Dogs received MT, 1.0, 3.0 or 10 mg/kg/day and ET, 3.0, 10 or 30 mg/kg/day. After 1 year, rats indicated that MT and ET were well tolerated at levels of 3.0 and 10 mg/kg. Side effects included: excessive salivation, slight erythema, hypersensitivity and muscle tenseness. At 30 mg/kg, appearance and behavior were altered, with more severe side effects, diminished weight gain and food consumption. Hematologic values of treated rats were comparable to control values. In dogs, MT and ET in doses of 3.0 and 10 mg/kg were well tolerated. Side effects in dogs included: occasional episodes of lacrimation, pupillary dilatation and slight mydriasis. At 30 mg/kg, side effects were exaggerated, with a wider range which included hyperactivity and slight ataxia. In all dogs body weights, hematologic, biochemical and urinary values remained within normal limits. Pathologic changes found at necropsy or under microscopic examination were not conclusively drug-induced. Evidence of adaptive tolerance to both drugs was apparent with both

rat and dog studies.

International Research and Development
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2172 Schievelbein, H., & Werle, E., Freisetzung von 5-Hydroxytryptamin durch Nicotin [Release of 5-hydroxytryptamine by nicotine.] Psychopharmacologia, 1962, 3, 35-43.

Nicotine (N) produces release of 5HT from rabbit thrombocytes (phosphate buffer pH 7.3; 37°C; 50 min.). This effect increases with increasing N-concentration. N at 1 mg/ml produces release of 58% of the total 5HT present. Temperature changes between 20 and 40°C have no effect on the reaction. There is no release below pH 6.7. Above pH 6.9 the release increases with increasing alkalinity. Sodium fluoride, EDTAA, 2,4-dinitrophenol and iproniazid (all at 0.001 mg/3 ml) did not affect the reaction but Natriumazid [sodium acetate?] produced slight inhibition. In a 10 times higher concentration N accelerates release of histamine from rat thrombocytes and from mast cells. Urinary excretion of 5HIAA increases in nonsmokers from 1.81 mg/24 hours to 3.03 mg/24 hours after smoking of 5-10 cigarettes in a day. The possible physiological significance of these observations is discussed.

Klinisch-Chemisches Institut
Chirurgische Klinik der Universität München
Munich, Germany

2173 Duchene-Marullaz, P., Busch, N., & Vacher, J. Toxicité aiguë, actions analgésique et sédatrice générale de quelques dérivés du crésotamide. [Acute toxicity, analgesic and general sedative actions of some cresotamide derivatives.] Thérapie, 1962, 17, 999-1004.

Eight substitution derivatives of cresotamide were studied for analgesic and sedative actions by means of electroshock pain to the dental pulp of rabbits. Three doses were used for each product: 250, 500 and 1000 mg/kg p.o. Also potentiation of pentobarbital narcosis was studied, using the

derivatives at 500 mg/kg p.o. and 100 mg/kg i.p. in mice. Effects of temperature regulation were studied in rats at 4°C; little modification was effected. Mice were tested on the turning rod 0.5 hours after the administration of 500 mg/kg p.o. doses. The LD₅₀'s p.o. were 1-3 g/kg, except for the chlorobenzoyloxy derivative which at 3 g/kg did not cause mortality. Most of the compounds possess analgesic activity superior to that of aspirin and sedative action is marked for allyloxy, butoxy and methoxy derivatives.

Route de Marsat
Riom, Puy-de-Dome
France

2174 Buchel, L., Levy, Jeanne, & Tissier, M. Contribution à l'étude pharmacologique du Triperidol (R. 2498). [Contribution to the pharmacologic study of triperidol (R 2498).] *Thérapie*, 1962, 17, 1053-1062.

The acute toxicity of triperidol was determined in Swiss mice i.v., i.p., i.m. and p.o. (stomach tube), and in Wistar rats i.m. and p.o. (stomach tube). LD₅₀'s for female mice were i.v.-17.4 mg/kg (aqueous solution) and 18.4 mg/kg (aqueous solution containing methyl and propyl paraoxybenzoates), i.p.-35.8 mg/kg, i.m. 64.0 mg/kg and p.o. 98.8 mg/kg. In rats the addition of paraoxybenzoate did not modify results. Male rats were more resistant to toxicity than females. The i.m. LD₅₀ in rats approximated 50 mg/kg while the p.o. LD₅₀ was approximately 3 times higher. In subacute 3-week and chronic 2-month toxicity studies (e.g., 2.5 mg/kg/day p.o. in young rats, none lost weight or died. Congestion of the hepatic veins after 3 weeks of treatment was noted at sacrifice. After 2 months congestion of the meninges and liver, with the presence of vacuolar cells was noted. These alterations regressed slightly after 2.5 months rest, and recovery is more marked in female than in male rats. The blood formula was not modified significantly in any instances.

15, rue de l'Ecole de Médecine
Paris VI°, France

2175 von Ledebur, I., Frommel, Ed., & Béguin, M. Nalorphine antagonism to the

narcotic action of chlorpromazine, meprobamate and metaminodiazepoxide (*Librium* *Medicina Experimentalis*, 1962, 7, 177-179)

The effect of 10 mg/kg nalorphine s.c. on the duration of sleep induced in guinea pigs by chlorpromazine (methaminodiazepoxide 30 mg/kg s.c.), meprobamate (100 mg/kg p.o.) and chlordiazepoxide (5 and 10 mg/kg p.o.) was elucidated. Nalorphine shortened the duration of sleep induced by these agents and therefore its action is not limited to interference with alkaloids. From the clinical standpoint, nalorphine might serve as an antidote to drugs acting on the reticular system, or even alleviate certain pathological states which inhibit this system.

Institut de Thérapeutique Experimentale
Ecole de Médecine
Geneva, Switzerland

2176 Hukuhara, T. Der Einfluss von Tranquilizern auf die elektrische Aktivität kortikaler und subkortikaler Substrate der Katze [The effect of tranquilizers on the electrical activity of the cortical and subcortical substrates of cats.] *Arzneimittel-Forschung* 1962, 12, 1133-1143.

EEG's obtained from 10 cats injected i.p. with 750-1000 mg/kg urethane, show phase alternation between the alerting pattern and the drowsy pattern, with a frequency of about 5-10 minutes, with a number of slow waves at 5/second, and an inhibition of the faster 30-40/second waves of the amygdaloid nucleus. Benactyzine (1-5 mg/kg i.v.) yielded similar results. Hydroxyzine (20-50 mg/kg i.v.) induces a transitory alerting pattern; the high-frequency activities are transformed into low-frequency waves, and the irregular oscillations in the hippocampus are increased. Meprobamate (25-50 mg/kg i.v.) also multiplies the low-frequency wave in the amygdaloid nucleus and the motor cortex, while the irregular activities in the hippocampus increase. Ectylurea (20-100 mg/kg i.v.) had no obvious effect. The EEG arousal reaction under electrical stimulation of the reticular formation was measured for the above-mentioned drugs and dosages. Urethane, benactyzine, hydroxyzine and meprobamate reduced the reaction induced by electrical stimulation of the reticulum.

amygdaloid nucleus, hippocampus, and motor cortex. Urethane and meprobamate cause a lowering of excitability so that arousal patterns at low activity levels may be observed. Low-frequency electric stimulation of the caput caudate nucleus resulted in an inhibition of the recruiting response in the motor cortex in about half of the animals. The effect of ectylurea on the response of the studied structures to electrical stimuli was negative. Although the behavioral patterns of animals are the same under tranquilizers as under barbiturates at low dosages, the electrical activity of the brain is considerably more strongly inhibited by barbiturates.

Pharmacological Institute of Tokyo University
Tokyo, Japan

2177 Vos, Th. De bepaling van glutethimide in serum. [The determination of glutethimide in serum] *Pharmaceutisch Weekblad*, 1962, 4, 517-524. Discussion, 524.

Improvements in the glutethimide determination method of Goldbaum and Williams (1960) are proposed: 1 ml of serum is diluted with an equal part of distilled water and treated as described by Algerie (1959), the extract being dried by shaking with 500 mg of anhydrous sodium sulphate after an acid wash. The residue after evaporation at 50°C. under vacuum is dissolved in 3.2 ml of 98% ethanol and 2.4 ml of this solution is pipetted into a 1 cm quartz cuvette. Then 0.8 ml of 0.2 N KOH is added, checking the time by means of a stopwatch. The mixture is stirred with a rod and the extinction measured in a Beckman D.U. spectrophotometer after 1, 2, 3, 4 and 5 minutes. Then 0.2 ml 1.6M. NH_4Cl is added in order to bring the pH down to about 9.7 and the extinction (due to the serum blank and basic glutethimide extinction) is measured once more. Recovery is ca. 95%. This determination is interfered with by bemegride, carbromal, bromeval and 4-isopropylantipyrine.

apotheek van het Algemeen Provinciaal Ziekenhuis- en Academisch Ziekenhuis te Groningen
Groningen, The Netherlands

2178 Kelemen, K., Magyar, K., & Knoll, J. Elektroenzephalographische Differenzierung von Sedato-Hypnotika und Major-Tranquillantien. [Electroencephalographic differentiation between sedative hypnotics and major tranquilizers.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 41-42. [Abstract]

The prolonged, reproducible, generalized EEG arousal reaction produced by the conditioned stimulus during the "spring test" in rats could not be inhibited even by high doses of sedatives or hypnotics (e.g., 40 mg/kg phenobarbital), but was prevented completely by low doses of the major tranquilizers (e.g., 1 mg/kg reserpine). These results confirm the specificity of the "spring test" for studies on the major tranquilizers and indicate that the nonextinguishing CR is facilitated by a specific condition in the reticular formation of the brain stem.

Institute of Pharmacology
Medical University of Budapest
Budapest, Hungary

2179 Kuhn, H.-F., & Friebe, H. Über den Nachweis von "Physical Dependence" bei Codein-behandelten Ratten. [Demonstration of "Physical Dependence" in codeine-treated rats.] *Medicina Experimentalis*, 1962, 6, 301-306.

Male Wistar rats received s.c. injections of codeine in increasing amounts for a period of 8 weeks. The total amount injected per animal was 2.3 g/kg in 8 weeks. After the last injection with codeine the rats received s.c. 20 mg/kg nalorphine, while another group of rats which received the same amount of nalorphine had received only 30 minutes prior to this injection an initial dose of 22.2 mg/kg codeine. Both groups were closely observed for 30 minutes after the injection, regarding reactions such as stretching, scratching, chewing, etc., on 1 hand, diarrhea, and increased or decreased locomotor activity on the other hand. Behavioral differences in the 2 groups were evident after 5 minutes. It is without doubt that chronic treatment with codeine produces in rats a condition in which the injection of nalorphine brings

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about a physical imbalance. The symptoms of nalorphine-induced acute abstinence are regarded as "physical dependence".

Pharmakologisches Institut
Universität Bonn
Bonn, Germany

2180 Carlsson, Arvid, & Hillarp, Nils-Ake. Formation of phenolic acids in brain after administration of 3,4-dihydroxyphenylalanine. *Acta Physiologica Scandinavica*, 1962, 55, 95-100.

The formation of 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) in rabbit brain following i.v. injection of DOPA (100 mg/kg body weight) was studied to gain further knowledge of the role of brain catechol-O-methyl transferase and MAO. After varying periods of time following DOPA administration, animals were killed and the brain was immediately removed and dissected. DOPAC was determined spectrophotofluorimetrically (by the method of Rosengren, 1960). HVA was estimated semiquantitatively by chromatography. As well, nialamide (100 mg/kg) and reserpine (5 mg/kg) were given i.v. 20 hours before DOPA injections. When DOPA was administered, large amounts of DOPA and HVA accumulated rapidly in the brain stem. This suggests that the dopamine formed endogenously from DOPA administration rapidly reaches sites of MAO, where DOPAC is formed which in turn reaches sites of catechol-O-methyl transferase. The data also suggests that the accumulated phenolic acids do not easily escape from the brain to the blood. The possibility of MAO being localized within the amine producing cell and the O-methyl transferase located extracellularly in the vicinity of supposed receptors, is discussed. In addition, iproniazid and nialamide prevent the formation of DOPAC from DOPA.

Department of Pharmacology
University of Göteborg
Göteborg, Sweden

2181 Walther, H. Die Wirkung von Anticholinergica auf den Strychnintremor in-

fantiler Mäuse. [The effect of anticholinergic agents on the strychnine tremor of infantile mice.] *Naturwissenschaften*, 1962, 49, 236-237.

Strychnine nitrate (1.0-1.2 mg/kg s.c.) induces in infant mice tremor of extremities and tail. The onset of the tremor is after ca. 5 minutes and lasts up to 1 hour, diminishing after 20-30 minutes. Noise or vibration can provoke and/or increase the tremor. The tremor can be completely suppressed with atropine or scopolamine (30 µg/kg). Phenobarbital influences the tremor only when given in large dose (40 mg/kg). Several phenothiazine derivatives, piperidinepropanol and benzhydrol were also found effective. Strychnine tremor in infant mice is proposed as a test method for drugs used in the treatment of parkinsonism.

Pharmakologisches Institut der
Medizinischen Akademie "Carl
Gustav Carus"
Dresden, Germany

2182 Gokhale, S.D., & Gulati, O.D. Nicotine convulsions and their modification by reserpine and chlorpromazine. *Indian Journal of Physiology and Pharmacology*, 1962, 6, 154-160.

Nicotine (1.0-1.5 mg/kg i.p.) was administered to 50 rats and a dose-response curve was obtained by plotting the convulsion rate against nicotine dosage. Since reserpine facilitated nicotine-induced convulsions while chlorpromazine antagonized them, reserpine (0.25-1.0 mg/kg i.p.) was injected 2 hours before the CD₂₀ (convulsive dose 20) of nicotine and chlorpromazine (1.0-3 mg/kg i.p.) was injected .5 hour before the CD₉₉ (convulsive dose 99) of nicotine. Nicotine (1-4 µg) was injected intracerebrally in 25 conscious male mice according to the method of Haley and McCormick (1957). Nicotine administered i.p. produced convulsions within 2-3 minutes and the dose-response curve indicated a CD₅₀ of 1.15 ± 0.15 mg/kg. Pretreatment with reserpine increased the convulsion rate after the CD₂₀ of nicotine according to dosage. The convulsive rate after the CD₉₉ of nicotine progressively decreased

When animals were pretreated with increasing doses of chlorpromazine. Intracerebral injection of minute amounts of nicotine caused immediate and violent convulsions in mice, directly related to nicotine dosage. Intracerebral CD₅₀ of nicotine was found to be $1.0 \pm 0.52 \mu\text{g}$.

Department of Pharmacology
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Varanasi, India

2183 Clouet, Doris H. The methylation of normorphine in rat brain. *Acta Neurologica Scandinavica*, 1962, 38, 26-27.

Morphine and codeine, and their demethylated nor-derivatives [See also Abstract 945] were isolated from rat tissue homogenates in incubation mixtures and identified by extraction followed by paper chromatography. In addition, when methyl donors labeled by C¹⁴ were used, the chromatographic strips were examined for radioactivity in a strip-counting autoscanner. Methionine labeled in the methyl group and reduced glutathione were incubated with normorphine, and morphine was recovered from the incubation mixture. Various liver preparations catalyzed the methylation of normorphine, including the supernatant of 0.25 M sucrose homogenate after centrifugation at 10,000 gravities for 20 minutes. A brain fraction prepared in the same way as liver methyltransferase was also effective in promoting normorphine methylation. With this brain preparation normorphine was methylated to codeine and morphine was also recovered, presumably by 3-demethylation of codeine. When S-adenosyl-methionine (C¹⁴-methyl) was substituted for methionine and the methionine activating enzyme, the pH optimum for the methylation of normorphine was 5.5. In vivo, no morphine methylation was demonstrated: methionine (C¹⁴-methyl) was injected into the cisterna magna of the rat (0.5 μM containing 2.5 μC of C¹⁴), and 15 minutes later 0.5 μM normorphine was administered by the same route. The rats were killed 10 minutes later and labeled morphine isolated from these brains. Therefore, with normorphine, remethylation of morphine is a possible metabolic step.

New York State Research Institute for
Neurochemistry and Drug Addiction
New York, N.Y.

2184 Winter, Charles A., & Flataker, Lars. Cage design as a factor influencing acute toxicity of respiratory depressant drugs in rats. *Toxicology and Applied Pharmacology*, 1962, 4, 650-655.

Young male rats received s.c. injections of morphine (18.75-150 mg/kg), anileridine (12.5-22.25 mg/kg) or pentobarbital (37.2-45 mg/kg) and were placed in open or shut cages. Two types of closed cages were used: 1 type with the bottom and 4 sides of sheet metal and the top of wire mesh, and the other type with the bottom and 1 wall of sheet metal, and the remaining 3 sides and top of wire mesh. The open cage consisted completely of wire mesh. When drugs were in effect and an animal was severely depressed, his nose would sometimes be pressed against a sheet metal surface and he would succumb, apparently in respiratory failure. More than a 10-fold increase in LD₅₀ could be obtained by placing animals in open cages as compared to sheet metal cages. Cages of wire mesh with sheet metal reinforcements and solid corners gave intermediate mortality figures. In sheet metal cages, deaths could be prevented either by shielding with wire mesh or moving the animal whenever his nose was pressed against a solid metal corner. Differences of the kind described in rats were not observed in mice injected with morphine or anileridine, a fact explainable by the hypermotility observed in mice during the peak effect of these drugs in contrast to the quiescence in rats.

Merck Institute for Therapeutic Research
West Point, Pa.

2185 Horovitz, Zola P., Chow, May-I, & Carlton, Peter L. Self-stimulation of the brain by cats: effects of imipramine, amphetamine and chlorpromazine. *Psychopharmacologia*, 1962, 3, 455-462.

Cats with electrodes in the lateral hypothalamus or caudate nucleus, which were

trained through a self-stimulation procedure (Horovitz et al., 1962), were tested 3 times a week and given i.p. injections of saline immediately before each 1 hour session. Before the 2nd session each week, various doses of imipramine (1-4 mg/kg), dexamphetamine (0.1-0.5 mg/kg), or chlorpromazine (2.5-5.0 mg/kg), were substituted for the saline. Doses were given in random order with at least 1 week intervening between drug injections. Dexamphetamine increased and chlorpromazine tended to decrease the response of cats working for stimulation of the caudate nucleus and lateral hypothalamus. In contrast, imipramine increased responses maintained by stimulation of lateral hypothalamic sites, but did not have a comparable effect on self-stimulation of the caudate. Thus, while all drugs altered rates of response maintained by lateral hypothalamic stimulation, only dexamphetamine and chlorpromazine produced comparable results on self-stimulation of both sites. Several postulates based on other studies are given for these results, including the suggestion that the site of imipramine activity differs from that of dexamphetamine and chlorpromazine in the cat, and imipramine activity may be restricted to hypothalamic structures.

Squibb Institute for Medical Research
New Brunswick, N.J.

2186 Hoffmeister, F. Über cerebrale polysynaptische Reflexe des Kaninchens und ihre Beeinflussbarkeit durch Pharmaka. [The cerebral polysynaptic reflexes in rabbits and their susceptibility to certain drugs.] Archives Internationales de Pharmacodynamie et de Thérapie, 1962, 139, 512-527.

The relation of pulse frequencies to strength of threshold signal, effects of resection of certain nerves, and effects of certain drugs upon the threshold signal were studied on more than 100 rabbits. The licking-reflex response to electrical stimulation of the upper incisors is extinguished by resection of the CNS on the mesencephalic and thalamic levels, but not on the prethalamic level. The jaw-opening reflex caused by electrical stimulation of the upper incisors is unaffected even by resections in the

mesencephalic area. The linguomandibular reflex threshold is lowered by resection at the mesencephalon. All of the tested drugs inhibit the licking-reflex of intact rabbits, with reserpine, chlorpromazine and butyrylperazine outranking in their effects, morphine, mephensine, phenylamidol and noramidopyrine sulfonate, in the above order. Onset of narcotic effects for the above drugs is at about 10-25% of the LD₅₀ dose. The hypnotic-narcotic glutethimide, methaqualone and hexobarbital are effective only at doses which produce paralysis. The jaw-opening reflex is inhibited by mephensine, phenylamidol, morphine, and chlorpromazine, the last named having the greatest effect. The linguomandibular reflex is blocked only by mephensine and phenylamidol.

Pharmakologisches Laboratorium
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Germany

2187 Essig, Carl F. Focal convulsions during barbiturate abstinence in dogs with cerebrocortical lesions. Psychopharmacologia, 1962, 3, 432-437.

Studies were made on 8 miniature dogs given increasing amounts of barbitol p.o. for 97-196 days until daily dose levels of 104-186 mg/kg were attained before abrupt withdrawal. Four dogs were used as controls and 4 received cortical lesions either before or during barbiturate intoxication as follows: aluminum hydroxide was injected into the cortex of 2 dogs at 5 punctate sites and in 2 others an ethyl chloride spray was applied to the exposed leptomeningeal surface until it became white and hard. For animals with aluminum hydroxide lesions a 2nd intoxication regimen was required because their final dose levels were appreciably lower than those of controls. In contrast to dogs with ethyl chloride induced lesions, dogs with aluminum hydroxide lesions manifested focal and generalized convulsions after drug withdrawal. Generalized convulsions did not all begin focally and their total incidence was either less than or equal to the number that occurred in control dogs. This indicated the independence of

local and generalized seizures as well as the fact that the former were either continuous or nearly so and the latter were episodic. These contrasts are compatible with the inference that the focal lesions may have been located in a functional system disparate enough from that operative in the generalized convulsions to discharge independently of the latter. Also, further postulations were made upon genesis of the above convulsions.

NIMH Addiction Research Center
USPHS Hospital
Lexington, Ky.

2188 Madan, B.R., Sharma, J.D., & Vyas, D.S. Some neuropharmacological actions of Librium. *Annals of Biochemistry and Experimental Medicine*, 1962, 22, 221-224.

Chlordiazepoxide (Librium), 5 mg/kg i.p., was given to 45 rats, while 45 controls received distilled water, 15 minutes before ethanol (2 g/kg) was injected i.p., after which loss and recovery of the righting reflex was recorded in order to determine potentiation of hypnosis. Pentobarbital hypnosis was determined in 70 rats by administering chlordiazepoxide (25 mg/kg i.p.) following induction of sleep by pentobarbital, 20 mg/kg i.p. To ascertain analgesic activity, chlordiazepoxide (25-100 mg/kg) was administered to 48 rats whose tails received painful stimulation from an electrically heated coil. To measure anticonvulsant activity, 60 rats were given 25-50 mg/kg i.p. of chlordiazepoxide 15 minutes before electroshock treatment, and 3 groups of 15 rats each received chlordiazepoxide (50 and 100 mg/kg i.p.) or water, 15 minutes after which pentetrazol was injected and animals were observed for twitching, for myoclonic convulsions, extensor tonic spasm and death. The same dosages were used to protect against seizures induced by picrotoxin and strychnine in 60 rats. Sleep prolongation occurred with ethanol and chlordiazepoxide, and the drug produced a significant increase in pentobarbital induced sleeping time. No significant analgesic activity was manifested by the drug. It exerted partial protective action against supramaximal shock but failed to completely protect animals against pentetrazol

shocks. Marked reduction in the severity of convulsions occurred at all dosage levels. No benefit was observed in picrotoxin or strychnine-induced seizures. The drug prevented development of the tonic extensor component produced by electroshock treatment.

Department of Pharmacology
Medical College
Bikaner, India

2189 Dandiya, P.C., Sharma, P.K., & Menon, M.K. Studies on central nervous system depressants. Part IV. Structure-activity relationship of some locally synthesized trimethoxy benzene derivatives. *Indian Journal of Medical Research*, 1962, 50, 750-760.

Fifteen trimethoxy benzene derivatives, differing from each other only in the relative positions of the methoxy group with respect to the side chain or in the structure of the side chain, were synthesized. Their influence on barbiturate hypnosis in mice, spontaneous activity in rats, CAR's in rats and effect on blood pressure in morphinized and urethanized dogs was studied. These compounds resemble reserpine and chlorpromazine in that they prolong pentobarbital hypnosis. None of the compounds influenced spontaneous motor activity. Only 2 compounds, 3,4,5-trimethoxy benzamide and its N-acetyl derivative were effective in influencing CAR's in trained rats. Most of the compounds caused a lowering of blood pressure in dogs.

Department of Pharmacology
S.M.S. Medical College
Jaipur, India

2190 Knecht, M., & Bernhard, K. Intensivierung der Demethylierung in vivo nach Angewöhnung. [Acceleration of demethylation in vivo after habituation.] *Helvetica Physiologica et Pharmacologica Acta*, 1962, 20, C34-C35.

When rats were fed small doses of glutethimide for 3 weeks and methyl-labeled N-methylglutethimide was then added to the microsome preparations from the rats'

livers, measurement of the radioactivity in the resultant formaldehyde showed that demethylation was going on at a much more rapid rate in the livers of habituated rats than in control animals. These results confirm the postulate that the reason for increased tolerance to drugs after prolonged use is stimulation of the activity of the catabolic enzymes.

Physiologisches-Chemisches Institut
Universität Basel
Basel, Switzerland

2191 Knoll, J., & Knoll, Berta. Methode zur tierexperimentellen Untersuchung von antidepressiv wirkenden Mitteln. [A method for animal experimentation with antidepressant drugs.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 41. [Abstract]

A procedure, based on the "spring test" for the major tranquilizers, is described for measuring the psychoenergetic activity of the clinically effective antidepressants in animals. While untreated rats generally jump up from a 45°C hotplate in 10-120", and those treated with reserpine (0.1 mg/kg) fail to jump up and eventually die, those given both reserpine and amphetamine (1 mg/kg), imipramine (5 mg/kg) or phenelzine (5 mg/kg) jump up even more rapidly than untreated controls.

Institute of Pharmacology
Medical University of Budapest
Budapest, Hungary

2192 Bättig, K. Wirkungen von Amphetamin auf verschiedene Schwimmleistungen der Ratte. [Effects of amphetamine on swimming capacity in rats.] *Helvetica Physiologica et Pharmacologica Acta*, 1962, 20, C15-C16.

The effect of amphetamine (1.5 and 4.0 mg per kg) on swimming time carrying a ballast of 10% of the body weight and on swimming speed (time to swim 4 m either free or against a load) was determined in male rats. The average swimming capacity was not improved by training but was increased 20-30% by amphetamine. The

swimming speed, however, was either unaffected by amphetamine (free swimming) or was reduced (swimming against a load); in contrast, there was a marked positive effect from training on the speed of swimming against a load. These results indicate that the effects of amphetamine are on motivation and not on neuromuscular ability, respiration or the cardiovascular system.

Institut für Hygiene und Arbeitsphysiologie
Eidgenössische Technische Hochschule
Zürich, Switzerland

2193 Kenedi, I., Kenéz, I., & Dávid, G. Die kardiovaskuläre Wirkung der experimentellen Amobarbitalwirkung. [Experiments on the cardiovascular effect of amobarbital.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 25. [Abstract]

The effect of the LD₅₀ of amobarbital on the ECG was studied in acute experiments on rats, the ECG changes being compared with the spontaneous daily changes observed during 5 days in the control group. In 60% of the cases there was sinus bradycardia, while 65% showed lengthening of the PQ interval and rare extrasystoles; none of these changes were noted in the control group. All of the animals survived, even following the most severe changes in the ECG. The effect on the ECG of a single large dose of spiractin, injected either at the same time as or 10 minutes after the amobarbital, was also studied in groups of 20 rats. In order to elucidate the pathogenesis of the ECG changes produced by amobarbital intoxication, the drug was administered after section of the vagus, the blood pressure was determined in a bloodless way, and the blood picture and urine volume were determined daily.

Health Service
Hungarian Peoples' Army
Budapest, Hungary

2194 Borswy, J., Vargha, L., & Kasztreiner, E. Untersuchung der Zusammenchemischer Struktur der Trioxazin-(N-3,4,5-trimethoxybenzoyl-morpholin) - Analoge.

The relationships between neurosedative effect and chemical structure in the tri-kazin- (N-3,4,5-trimethoxybenzoyl-morpholin) -analogues.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 43-44. [Abstract]

The i.p. toxicity, neuroplegic activity and analgesic effects of a number of analogues of N- 3,4,5- trimethoxybenzoylmorpholine were determined in mice. Any change in the number, position and size of the methoxy groups led to a decrease in the analgesic and neurosedative activity, as did breakage of the morpholine ring or lengthening of the aliphatic chain. Aliphatic substitution on the morpholine ring increased the analgesic effect while the tranquilizing effect was unchanged.

Drug Industry Research Institute
Budapest, Hungary

2195 Smith, Barbara. The distribution of monoamine oxidase in the brain and pituitary gland of the albino rat. *Acta Neurologica Scandinavica*, 1962, 38, 52-53.

Vitro-B.T. and M.T.T. tetrazolium salts were used to localize MAO activity in the brain and pituitary gland of the rat. Detectable activity was divided into 3 grades: background perivascular activity; highly vascular gray matter activity, and white matter activity. The highest activity was observed in the posterior lobe and neural stalk of the pituitary gland, the supra-optic and paraventricular hypothalamic nuclei, the peri-ventricular gray matter, fasciculus retroflexus, interpeduncular nucleus, dorsal tegmental nucleus and part of the mesencephalic root of the trigeminal nucleus. Histochemical analyses of levamethamphetamine and 5HT content were made on brain sections from animals which had received an MAO inhibitor, but substrate concentration failed to reach detectable levels.

Maida Vale Hospital for Nervous Diseases
London, Great Britain

2196 Barankay, T., Pórszász-Gibisz, E., Katalin, & Pórszász, J. Über elektro-

physiologische Unterschiede im Wirkungsmechanismus einiger Muskelrelaxantien. [The electrophysiological differences in the mechanism of action of some muscle relaxants.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 44-45. [Abstract]

Recordings of the action potential of individual muscle spindle afferents had γ -efferents isolated from the lumbar spine (L5-S1) of cats showed that the activity of the γ -efferents was inhibited for several hours by 1 mg/kg of chlorpromazine but was unaffected by Mydeton (10 mg/kg i.v.). Neither drug had any effect on the muscle spindle receptors, even at high doses. Since Mydeton does not inhibit the monosynaptic patellar reflex and has no curariform activity, the muscular weakness after Mydeton administration must be due mainly to depression of the multisynaptic connections in the spine.

Institute of Physiology
Medical University of Szeged
Szeged, Hungary

2197 Werboff, Jack, & Dembicki, Eugene L. Toxic effects of tranquilizers administered to gravid rats. *Journal of Neuropsychiatry*, 1962, 4, 87-91.

Reserpine (0.1 mg/kg s.c. in 3 divided doses), chlorpromazine (6.0 mg/kg/day s.c. in 3 divided doses), meprobamate (60.0 mg/kg/day s.c. in 3 divided doses) or distilled water was administered to 89 gravid Sprague-Dawley rats during gestation on either days 5 through 8, 11 to 14 or 17 to 20. Daily observations for neonatal mortality were made for 21 days from birth through weaning. Weight was recorded at regular intervals for 120 days. Mortality was classified 3 ways; born dead, died on days 1 through 21, or devoured by mother. The 89 gravid rats delivered a total of 869 animals, 279 of which failed to survive. Neonatal mortality with drugs administered during the 1st trimester was: 27.1% with reserpine, 43.9% with chlorpromazine, 48.0% with meprobamate and 19.2% with controls. Drugs in the 2nd trimester yielded: 36.8% with reserpine, 11.7% chlorpromazine, 35.4% meprobamate and 10.6%

controls. Mortality figures for the 3rd trimester were: 25.0% reserpine, 61.6% chlorpromazine, 45.6% meprobamate and 7.3% controls. These tranquilizers administered to the gravid rat are toxic to the embryos and to the newborn. The largest contributor to the high neonatal mortality in the drug groups was the devoured by mother category. Reserpine and meprobamate-treated offspring weighed less than controls, while chlorpromazine-treated offspring weighed more than controls.

University of Madrid
Madrid, Spain

2198 van der Schoot, J.V., Ariëns, E.J., van Rossum, J.M., & Hurkmans, Th. M. Phenylisopropylamine derivatives, structure and action. *Arzneimittel-Forschung*, 1962, 12, 902-907.

Amphetamine (phenylisopropylamine) and a large number of its derivatives were tested, using spontaneous activity in mice (interruptions of photoelectric cell light beams per minute). A dose-effect curve was worked out for amphetamine at 10, 15, 20 and 25 μ M/kg i.p. for use as a reference. Also several α -sympatholytic and β -sympatholytic compounds were used. The replacement of the phenyl ring in amphetamine by certain 5- or 6-membered rings is allowed. The binding of the amino group to a secondary carbon atom seems to be required. The chain between the amino group and the ring is restricted to 2 carbon units. The introduction of substituents results in a decrease or a loss of activity. A relatively wide variation of substituents in the side chain and even an incorporation of an amino group in the aliphatic ring is tolerated. The introduction of OH groups in the phenyl ring leads to a definite loss of activity. The introduction of other small substituents in the phenyl ring is tolerated in the para and meta positions. Substitution in the ortho position leads to a loss of activity. All reasonably active compounds have an amino group attached to a secondary carbon atom. For some compounds closely related to amphetamine, a direct action on cerebral catecholamine receptors is feasible, while for a number of N-substituted amphetamines and cocaine an indirect action

based on the liberation of cerebral catecholamines is suggested as a possible mechanism of action.

Pharmacological Institute
R.C. University
Nijmegen, The Netherlands

2199 Airaksinen, M.M., & Mattila, M. The sedative and lethal actions of reserpine in mice, as modified by 5-hydroxytryptophan, 3, 4-dihydroxyphenylalanine, methylphenidate, and nikethamide in cold and warm environments. *Acta Pharmacologica et Toxicologica*, 1962, 19, 199-204.

The effect of DOPA (3,4-dihydroxyphenylalanine), 5HTP and some stimulants on the sedative and lethal action of reserpine in mice in cold (9°C) and warm (37°C) environments is discussed. The reserpine dose was 2 mg/kg, as a single dose or 1 mg/day on 2 consecutive days. Some animals received 200 mg/kg DOPA or 5HTP, separately or together 3 times at intervals of 3-4 hours; some received 50 mg/kg nikethamide or 25 mg/kg methylphenidate similarly. In the cold, half of the reserpinized mice died in 8 hours and all in 24 hours. Sedative action in the cold was almost the same when reserpine was administered in the cold or before the beginning of the experiment. In the warm environment, most of the mice died in 24 hours; convulsions were common, and sedation was slight and infrequent. Without reserpine, 5HTP was lethal to half the mice. As in the cold, it greatly increased reserpine toxicity. This 5HTP effect was partially antagonized by DOPA; when given alone DOPA had no effect upon reserpine toxicity. Only methylphenidate was very toxic in the warmth. Also it greatly enhanced reserpine lethality, while the nikethamide was inactive.

Department of Pharmacology
University of Helsinki
Helsinki, Finland

2200 Milthers, Kirsten. The *in vivo* transformation of morphine and nalorphine into normorphine in the brain of rats. *Acta Pharmacologica et Toxicologica*, 1962, 19,

5-240.

anesthetized rats were given aqueous solutions of either morphine or nalorphine (10 mg/ml) i.v. in amounts of 100 mg/kg. The rats were killed 15 minutes later for determinations of morphine, nalorphine and normorphine. Concentrations of the substances in blood and in brain tissue were determined; the average recoveries of morphine, nalorphine and normorphine were 90, 96 and 72% respectively. Normorphine could not be demonstrated in the brain of normal rats given 100 mg/kg morphine; the morphine concentration in these brains was only 7.1 µg/g and the average concentration of morphine and normorphine in the blood was 62 µg/ml and 3.8 µg/ml respectively. N-dealkylation of morphine occurs more readily than that of nalorphine in the brain of rats.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

201 Jöhanncsson, Torkell, & Milthers, Kirsten. Morphine and normorphine in the brain of rats. A comparison of subcutaneous, intraperitoneal, and intravenous administration. *Acta Pharmacologica et Toxicologica*, 1962, 19, 241-246.

Morphine or normorphine was administered (100 mg/kg s.c., 500 mg/kg i.p. or 50 mg/kg i.v.) to rats, which were killed 15 minutes after the injection. Morphine was found in the brain in higher amounts than normorphine when the subcutaneous and intraperitoneal route had been used. When given intravenously, both drugs were found at the same concentrations in the brain. The lower concentration of normorphine than of morphine in the brain may be explained by a greater self-depression of the absorption of normorphine. Both drugs have equal analgesic potency.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

202 Jöhanncsson, Torkell. The concentrations of morphine in the brains of rats

receiving morphine and neostigmine. *Acta Pharmacologica et Toxicologica*, 1962, 19, 286-292.

Morphine (700 mg/kg) and neostigmine (0.2 mg/kg) were given i.p. to morphine-tolerant and nontolerant male rats. Spontaneous death after i.p. injection of both drugs occurred 14-26 minutes later. For comparison, the rats given morphine alone were killed at about the same times as those at which the rats died from the combined injections. Morphine was determined in the brains of both groups. Neostigmine was not found to increase the amounts of brain morphine. The simultaneous i.p. administration of both drugs can lead to an erroneous determination of morphine. However this was overcome when paper chromatography was included in the analytical procedure and the error was not met with during the analysis of the brains of the tolerant rats.

Department of Pharmacology
University of Copenhagen
Copenhagen, Denmark

2203 Frahm, Margarete, Löbkens, K., & Soehring, K. Der Einfluss subchronischer Alkoholgaben auf die Barbiturat-Narkose von Meerschweinchen. [The influence of subchronic administration of alcohol on barbiturate narcosis in guinea pigs.] *Arzneimittel-Forschung*, 1962, 12, 1055-1056.

Ethyl alcohol solutions of 5, 10 or 15% were given to guinea pigs as the only source of liquid over a period of 14 days. The onset and duration of narcosis with pentobarbital (20 mg/kg), methitural (70 mg per kg) and hexobarbital (50 mg/kg) were measured at intervals of 7 days. The onset of narcosis is slightly prolonged in proportion to the concentration of alcohol ingested. In contrast, the duration of narcosis was considerably reduced in proportion to the concentration of alcohol in all 3 series of experiments. Measurements taken 14 days after discontinuation of the alcohol ingestion showed a return to normal values.

Pharmakologisches Institut
Universität Hamburg
Hamburg, Germany

Pharmacology
Abstract 2204

2204 Pletscher, A., & Gey, K.F. Action of imipramine and amitriptyline on cerebral monoamines as compared with chlorpromazine. *Medicina Experimentalis*, 1962, 6, 165-168.

Wistar rats were pretreated with varying doses of imipramine, amitriptyline and chlorpromazine i.p. One hour later the animals received 2 mg/kg reserpine or 100 mg/kg iproniazid s.c. Rats receiving 1 drug only or no drug at all served as controls. Brain levels of 5HT or of 5HT and levarterenol were determined 4 hours after administration of iproniazid and reserpine respectively using spectrophotofluorometric methods. Furthermore, rats pretreated with chlorpromazine or imipramine 1 hour before injection of 5HTP were sacrificed half an hour later and the following procedures were carried out: a/ immediate homogenization of the brains and spectrophotofluorometric assay of 5HT (5HT rise in vivo) and b/ incubation of the

isolated intact brains in wet chambers for 2 hours at 37°C before homogenization and c/ determination of the 5HT rise occurring post mortem. Imipramine, amitriptyline and chlorpromazine have no effect on endogenous 5HT and levarterenol. The iproniazid-induced 5HT rise was not influenced by imipramine and amitriptyline even at high doses (50 mg/kg). Also 20 mg/kg dose of these drugs had no or only a slight effect on reserpine-induced decrease of 5HT and levarterenol whereas 50 mg/kg imipramine and amitriptyline counteracted the reserpine effect. Chlorpromazine diminished the above mentioned actions of iproniazid and reserpine at 20 mg/kg and less. Thus sedation seems to be parallel to interference with monoamine metabolism.

Medical Research Department
F. Hoffmann-LaRoche and Co., Ltd.
Basel, Switzerland

See also 2035, 2100, 2122, 2135, 2205, 2218, 2220, 2221, 2227, 2228, 2230

2205 Vasbinder, H., & van der Sijde, H.R. Een gevoelige kleurreactie op imipramine. [A selective color reaction for imipramine.] *Pharmaceutische Weekblad*, 1962, 7, 610-611.

Imipramine reacts in the diphenylamine test for nitrates and nitrites by forming a colorless solution in acidified (H_2SO_4) solutions and a dark blue color in alkaline solutions ($NaNO_3$). Also acidic and basic diphenylamine colors were given for chlordiazepoxide, haloperidol, hydroxyzine, mephenesin, meprobamate, chlorpromazine, levomepromazine, mepazine, perphenazine, prochlorperazine, promethazine, promazine and thiazinaminum.

Geneesmiddelen Apotheek
Amsterdam, The Netherlands

2206 Kamp, W., Klijsen, J.B., & Ruward, H. De scheiding van enige barbitalen met behulp van een anionuitwisselaar op ionenbasis. [Separation of some barbiturates by means of anion exchange resins.] *Pharmaceutische Weekblad*, 1962, 6, 889-894.

Separation of 11 barbituric acid derivatives was accomplished. About 50 mg of the barbiturates were dissolved in 10 ml 1 N NH_3 and passed through a 10 x 250 mm column of Dowex 1-X2 (100-200 mesh) in the acetate form. After washing with 3 x 10 ml water, the acids were eluted with 0.1 M NH_4COOH buffer solutions at pH 1, which contained different concentrations of methanol. A number of mixtures were analyzed, including Solutio Barbamini (allobarbital and barbital) and Iniectio Barbamini (acrobital and barbital).

Pharmaceutische Laboratorium der
Rijksuniversiteit
Groningen, The Netherlands

2207 van Haeringen, A. De bepaling van barbituraten in bloed en urine. [The determination of barbiturates in serum and urine.] *Pharmaceutisch Weekblad*, 1962, 7, 173-190.

for the UV spectrophotometric determina-

tion of barbiturates in body fluids, extraction in an acid medium followed by the measurement of optical density at 240 mμ, at both pH 2 and pH 10 is the method of choice. Sulfonamides and salicylates may significantly interfere with the determination and these interferences are difficult to correct. With urine samples, careful purification and extraction is necessary. A method for quantitative determination in sera, and qualitative estimations in urine samples is given.

Klinisch Chemisch Laboratorium
Psychiatrische Inrichting "Dennenoord"
Zuidlaren, The Netherlands

2208 Fournel, J. Dosage de l'acide phénylpyruvique urinaire en présence de lévomépromazine (7.044 RP). [The assay of phenylpyruvic acid in the presence of levomepromazine (RP7-044).] *Annales de Biologie Clinique*, 1962, 20, 659-663.

An assay method was worked out for urinary phenylpyruvic acid in patients under treatment with levomepromazine. Phenylpyruvic acid was separated from levomepromazine by acidic ether extraction (the phenothiazines and their metabolites remained in the aqueous phase). Colorimetric determination is then made by means of the addition of ferric chloride (640 mμ). The method is sufficiently precise to evaluate phenylketonuria in oligophrenics treated with levomepromazine or other amines derived from phenothiazine.

Société des Usines Chimiques Rhône-Poulenc
Laboratoires de Recherches
Vitry-sur-Seine, France

2209 Bernsohn, Joseph, Custod, James T., Remenchik, Alexander P., & Talso, Peter J. High energy phosphate compounds in erythrocytes from schizophrenic and non-schizophrenic subjects. *Journal of Neuropsychiatry*, 1962, 4, 22-27.

Samples of venous blood from 12 schizophrenic patients, 4 nonschizophrenic psychiatric patients and 6 clinically healthy subjects were used to measure the rate of

P³² incorporation by erythrocytes into various high energy phosphate compounds and to determine erythrocytic ATP levels. Chlorpromazine [dosage unspecified] was administered to psychiatric patients, and all biological determinations were performed within 2-3 weeks of hospitalization. The blood samples were incubated and centrifuged, after which blood nucleotides were eluted; values were obtained for erythrocytic levels of inorganic phosphate hexosediphosphate, ADP and ATP. Analysis of variance on the resultant data revealed no significant difference between the control group and nonschizophrenics. Therefore, these 2 groups were combined. No statistically significant differences occurred between schizophrenics and controls with respect to inorganic phosphate, hexosediphosphate and ADP. Comparison of the schizophrenic group with the control group revealed significant differences in ATP level. Thus ATP accumulates in the erythrocyte of the schizophrenic at a rate in excess of that in the normal persons.

Stritch School of Medicine
Loyola University
Chicago, Ill.

2210 Vander Kamp, Harry. Nuclear changes in the white blood cells of patients with schizophrenic reaction. *Journal of Neuropsychiatry*, 1962, 4, 1-3.

Blood samples from 40 normal people and 60 chronic schizophrenics was centrifuged, air dried, fixed and stained with Masson's trichrome stain. Color photographs of the resultant slides revealed that lymphocytic nuclei in schizophrenics stained black to dark purple and that chromatin lacked even distribution, showed marked variation in density and lacked an organized pattern. These differences lacked clarity when Wright's stain was substituted. The Feulgen reaction also demonstrated the difference in chromatinic density and in distribution. The periodic acid-Schiff procedure indicated that more glycoprotein granules were present in the cytoplasm of the lymphocyte in the schizophrenic person than in the normal individual. Consulting hematologists and histochemists state that variations may be anticipated in other blood

cell nuclei and even in the nuclear patterns of cells of various tissues and organ.

VA Hospital
Battle Creek, Mich.

2211 Mukai, Akira, & Ejima, Tatsunori. Studies on sialic acid (neuraminic acid) in cerebrospinal fluid. Part 3: Methodology of determination by Bial's reaction. *Tohoku Journal of Experimental Medicine*, 1962, 77, 223-229.

Bogoch's (1957) method (the Bial's reaction) was used in the study of neuraminic acid concentration in CSF samples. Both whole and protein-free CSF samples were tested. Assay of the free neuraminic acid fraction is inconstant and a large part of neuraminic acid is in protein-bound form.

Department of Neuropsychiatry
Tohoku University School of Medicine
Sendai, Japan

2212 Mukai, Akira, & Ejima, Tatsunori. Studies on sialic acid (neuraminic acid) in cerebrospinal fluid. Part 4: Methodology of determination by diphenylamine reaction. *Tohoku Journal of Experimental Medicine*, 1962, 77, 230-238.

The diphenylamine reaction was used for the estimation of neuraminic acid in CSF samples. The reaction is unsatisfactory except in the estimation of acid content in CSF protein or in the Niazi-State's (protein-free, ethanol-precipitated) fraction. In the cases where TCA is present the blue or indigo-blue coloration tends to intensify, interfering with analysis both at 530 m μ and 660 m μ . There is several times as much neuraminic acid in the protein-bound fraction as in the protein-free samples.

Department of Neuropsychiatry
Tohoku University School of Medicine
Sendai, Japan

2213 Mukai, Akira, & Ejima, Tatsunori. Studies on sialic acid (neuraminic acid) in cerebrospinal fluid. Part 5: Protein-bound

lic acid in cerebrospinal fluid in mental disorders. Tohoku Journal of Experimental Medicine, 1962, 77, 343-351.

CSF samples from 37 schizophrenics, 5 cases of depression, 1 mania, 2 epilepsy, chronic alcoholism, 3 general paralysis, senility and 9 control subjects were assessed. The diphenylamine method was used on whole CSF, TCA-precipitated CSF and ethanol-precipitated CSF. In the control group, the neuraminic acid content averaged ca. 0.218 and ratio of acid (mg%) to total protein (0.1%) was 109:100; in schizophrenic subjects the figures were id., ca. 0.267 and 92.1:100; in depression, ibid., ca. 0.278 and 74.5:100; in alcoholism ibid., ca. 0.321 and 107:100, and in mania the ratio was 49.6:100. In the other brain organic diseases, the neuraminic acid concentration was found raised. In mania there is a tendency towards an increase in neuraminic acid through an imbalance of the mechanisms of its production.

Department of Neuropsychiatry
Tohoku University School of Medicine
Sendai, Japan

2214 Mukai, Akira, & Ejima, Tatsunori. Studies on sialic acid (neuraminic acid) in cerebrospinal fluid. Part 2: Methodology of determination by direct Ehrlich reaction. Tohoku Journal of Experimental Medicine, 1962, 77, 128-135.

The direct Ehrlich method was used for the determination of neuraminic acid in CSF and found clearly less useful than Bogoch's reaction using diphenylamine; it is not suitable for protein-free samples which contain TCA, however it may be suitable for the determination of neuraminic acid in whole CSF samples or protein-free CSF which does not contain TCA. The existence of a large amount of free neuraminic acid compared to protein-bound neuraminic acid in CSF is denied.

Department of Neuropsychiatry
Tohoku University School of Medicine
Sendai, Japan

2215 Mukai, Akira, & Ejima, Tatsunori. Studies on sialic acid (neuraminic acid) in cerebrospinal fluid. Part 1: Total bial-positive substance in cerebrospinal fluid in schizophrenic subjects. Tohoku Journal of Experimental Medicine, 1962, 77, 120-127.

Bial-positive substance (total neuraminic acid by Bogoch's 1958 method) was assessed in CSF samples from 46 schizophrenics and 25 other patients with various mental disorders. Also the diphenylamine reaction was used on protein-free (ethanol-precipitated) CSF. In the schizophrenic subjects the concentrations of neuraminic acid in CSF averaged ca. 48.2, while in manic-depressive psychoses it averaged ca. 46.0. In the control group (neuroses) it averaged ca. 46.0, while in mental and nervous disorders caused by somatic illness the figure was 45.1 $\mu\text{g/ml}$. No tendency of the low neuraminic acid concentration appeared in schizophrenic subjects compared to the control group or other mental and nervous disorders. No characteristic relationship could be established between the total neuraminic acid and total protein or protein-bound neuraminic acid in the CSF.

Department of Neuropsychiatry
Tohoku University School of Medicine
Sendai, Japan

2216 Jensen, Knud. Paper chromatographic determination of indoles in human cerebrospinal fluid. Acta Neurologica Scandinavica, 1962, 38, 278-284.

CSF samples were obtained from a general hospital and extracted with acetone-ether after saturation with sodium chloride (Nakai 1958). The solvent residue was taken up in methanol-acetone and used for paper chromatographic analysis of indoles. The amount of indoles extracted from pooled fluid was estimated semiquantitatively from the size and intensity of the spots on the chromatogram. The following indoles could be detected in human CSF: tryptamine, indol-3-acetic acid, tryptophan and 5 HIAA.

Neurochemical Research Unit
State Mental Hospital
Risskov, Denmark

2217 Bonta, I. L., Wijmenga, H. G., & Hohensee, F. The action of substance P and other brain extracts on the central nervous system. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 265.

CNS depressant activity of crude preparations containing substance P [no details] were confirmed, using the exploratory behavior test and i.v. strychnine titration. However, other subfractions of hog-brain extracted according to methods employed for substance P, but devoid of ileum-contracting properties, displayed comparable inhibition of the CNS.

Pharmacological Research Department
N.V. Organon, Oss
Amsterdam, The Netherlands

2218 Rajeswaran, Ponnusamy, & Kirk, Paul L. Tranquillizing and related drugs: properties for their identification (part III). *Bulletin on Narcotics*, 1962, 14, 19-33.

X-ray diffraction has been successfully utilized with the study and identification of alkaloids, barbiturates, analgesics, sedatives and anticonvulsants. A total of 46 compounds were examined, using a copper-K α -radiation X-ray spectrometer equipped with a recording potentiometer. Phenothiazine derivatives; reserpine and related alkaloids; diphenyl methane derivatives; substituted butanediols; ureides, amides, hydrazines and related compounds, and miscellaneous compounds were detailed. Additionally UV spectrum absorption data on these drugs is given.

School of Criminology
University of California
Berkeley, Calif.

2219 Roberts, Eugene. Enzymology and function of the γ -aminobutyric acid system. *Acta Neurologica Scandinavica*, 1962, 38, 19.

Experiments were performed on laboratory animals in which correlations were sought between the electrophysiological measurements and GABA levels, and the activities of the related enzymes in various areas

of the brain. Primary biological material was the optic lobe of the chick in which there are progressive increases in various components of the GABA system with age. GABA can be physically bound to particulate fraction of brain by a process not requiring energy but dependent on the presence of sodium ions. Some results obtained by density gradient centrifugation have shown that the nondiffusible and easily extracted GABA is associated largely with the nonmitochondrial particulate fractions. Glutamic acid decarboxylase activity may be present in neurons, while GABA- α K transaminase activity may be present in glial or other nonneuronal elements. The relative rates of decarboxylation and transamination in a particular cerebral area may determine GABA levels.

Department of Biochemistry
Medical Research Institute
City of Hope Medical Center
Duarte, Calif.

2220 Paoletti, Pietro, Grossi, Enrica, Fumagalli, Remo. The effect of psychotropic agents on brain lipid biosynthesis and metabolism. *Acta Neurologica Scandinavica*, 1962, 38, Suppl. 1, 37-38.

Imipramine and demethylimipramine at levels as low as 10^{-5} M stimulated incorporation of C^{14} acetate into the fatty acids of brain phospholipids in vitro without effecting the biosynthesis of cholesterol or the fatty acids of neutral fat. In vivo administration of demethylimipramine, 3.4 mg/kg, stimulated brain phospholipid fatty acid synthesis while imipramine exhibited a less marked and delayed effect. In order to investigate fatty acid turnover of brain phospholipids, newborn rats received injections of C^{14} acetate after which single fatty acids were isolated from brain phospholipids and assayed for specific radioactivity at 1-3 days after labeled acetate administration. The effect of demethylimipramine treatment in these experiments will be evaluated. Other work relevant to the effects of chlorpromazine, azacyclonol, pipradol and 2-dimethylaminoethanol on brain lipids is also mentioned.

University of Milan
Milan, Italy

2221 Wollemann, Mária, Elödi, P., & Kelecsani, T. Über den Mechanismus der Phenothiazin-Dehydrogenase-Hemmung. [The mechanism of the inhibition of dehydrogenase by phenothiazines.] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 20, 12. [Abstract]

The effect of various phenothiazines and their oxidation products on dehydrogenase activity was studied in vitro, the oxidation products being obtained by means of ceric sulfate or photooxidation and identified by absorption spectrophotometry. If chlorpromazine at a concentration of 10^{-5} M is exposed to light for 20-30 minutes in the presence of alcohol- or phosphoglycerdehyde-dehydrogenase, enzymatic activity is inhibited 70-80% and the absorption spectrum of the chlorpromazine is altered in the direction of a flatter curve. A partially oxidized intermediate (chlorpromazine-X), with an immediate inhibitory effect on dehydrogenase activity, has been isolated using ceric sulfate. The inhibitory effect of this intermediate is stronger than that of the more completely oxidized chlorpromazine sulfoxide.

Institute of Biochemistry
Hungarian Academy of Sciences
Budapest, Hungary

2222 Davis, Richard B. Oxidation of homogentisic acid by nitrous acid and its interference on the determination of 5-hydroxyindoleacetic acid. *Clinical Chemistry*, 1962, 6, 660-664.

No color reaction was observed in the determination of urinary 5HIAA from a patient with alkaptonuria and ochronosis. Further investigation showed that homogentisic acid is oxidized preferentially by nitrous acid, and if present in sufficient amounts prevents the α -nitroso- β -naphthol reaction with 5HIAA, i.e., oxidation of homogentisic acid to the corresponding phenol occurs in the presence of developers used for the 5HIAA reaction. With amounts of homogentisic acid well below those secreted in alkaptonuria, significant interference with the tests occurred. Compounds related to homogentisic acid, including homogentisic lactone, o-hydroxyphenylace-

tic acid and p-hydroxyphenylpyruvic acid do not form a product giving interference near 250 m μ in concentrations as great as 200 mg/liter. Also ascorbic acid interferes with the color reaction for 5HIAA when added to the buffer before the developer (ascorbic acid was capable of partial reduction of 1,4 benzoquinone-2-acetic acid to homogentisic acid).

Department of Medicine
University of Minnesota Medical School
Minneapolis, Minn.

2223 Paasonen, M.K., & Kivalo, E. The inactivation of 5-hydroxytryptamine by blood platelets in mental deficiency with elevated serum 5-hydroxytryptamine. *Psychopharmacologia*, 1962, 3, 188-192.

Blood was collected from mentally retarded children (mongolism, cerebral palsy and encephalopathy) or young adults and the inactivation of 5HT was measured by the disappearance of 5HT during incubation of platelet-rich plasma with or without 20 μ g/ml tetrabenazine. The mentally defective patients were divided into 2 groups according to the 5HT content in serum. In the 1st ("normal") group were those with values <200 ng/ml (6 mongolism, 4 cerebral palsy) and in the 2nd those with values >200 ng/ml (7 cerebral palsy, 5 encephalopathy). The content of 5HT per platelet was twice as high in the 2nd than in the 1st group. When the platelet-rich plasma was incubated with tetrabenazine in vitro equal amounts of 5HT were liberated from platelets from both groups. During the liberation slightly more 5HT was inactivated in the 1st group than in the 2nd. The ability of platelets to inactivate 5HT under these conditions does not explain the higher serum and platelet values found in some patients.

Department of Pharmacology
University of Helsinki
Helsinki, Finland

2224 Horita, A., & Weber, L.J. Dephosphorylation of psilocybin in the intact mouse. *Toxicology and Applied Pharmacology*, 1962, 4, 730-737.

Male mice received psilocybin (100 mg/kg i.p.) and psilocin (72 mg/kg i.p.), preceded in some instances by sodium β -glycerophosphate (45 mg) administered as a competitive substrate 5 minutes before drug administration. The mice were sacrificed at 5 minute intervals after which the brain, liver and kidney tissue was homogenized. Resultant homogenates were analyzed for psilocin content. Behavioral changes were recorded before sacrifice. After psilocybin injection, measurable amounts of psilocin occurred in liver and kidney tissue in 5 minutes and peak levels were observed in 10-20 minutes, while peak brain levels occurred in 25-30 minutes. Psilocin levels were highest in kidney tissue and lowest in brain. Animals treated with psilocybin evidenced piloerection, exophthalmos, hind-leg ataxia and depression which gradually disappeared in 3-4 hours. Pretreatment with sodium β -glycerophosphate markedly reduced the accumulation of psilocin in all tissues and attenuated behavioral effects. Tissue concentrations of psilocin after psilocin administration were considerably higher than those observed with psilocybin. Psilocin given to mice pretreated with sodium β -glycerophosphate yielded tissue concentrations which approximated those in normal psilocin-treated animals. Psilocybin was obviously dephosphorylated to psilocin in the intact mouse. Psilocybin exerts CNS effects only after dephosphorylation since the amount of brain psilocin is much lower after treatment with sodium β -glycerophosphate.

Department of Pharmacology
School of Medicine
University of Washington
Seattle 5, Wash.

2225 Culley, W.J., Mertz, E.T., Luce, M.W., Calandro, J.M., & Jolly, D.H. Paper chromatographic estimation of phenylalanine and tyrosine using finger-tip blood. Its application to phenylketonuria. *Clinical Chemistry*, 1962, 8, 266-269.

Using a paper chromatographic method for the determination of serum phenylalanine and tyrosine which requires 0.12 ml of serum from finger-tip blood, no deproteinization and no expensive equipment, 15

phenylketonurics and 5 fasting nonphenylketonurics were tested to establish serum phenylalanine and tyrosine levels. In phenylketonurics, the average serum phenylalanine level was 29 mg/100 ml, and the tyrosine level 1.3 mg/100 ml. Nonphenylketonurics averaged 2 mg/100 ml serum phenylalanine and 1.4 mg/100 ml tyrosine. Independent chromatogram evaluations were carried out on sera from 3 phenylketonurics by 6 investigators (4 of whom had no experience reading chromatograms). Averages obtained by the 6 investigators range from 22.3-32.5 mg/100 ml phenylalanine. An expert ran 4 chromatograms on one phenylketonuric which yielded an average of 20 mg/100 ml of serum phenylalanine. A similar experiment with serum from other phenylketonurics resulted in values averaging 28-32.5 mg/100 ml. This chromatographic technique was used to follow serum phenylalanine levels in 2 phenylketonurics from the day they began a low phenylalanine diet until they were taken off the diet and the serum phenylalanine level returned to the uncontrolled state.

Mental Retardation Research Laboratory
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Butler, Ind.

2226 Winne, D. Der Abbau von Hexobarbital in vivo bei ganzkörperbestrahlten Mäusen. [The catabolism of hexobarbital in mice following total body irradiation] *Archiv für Experimentelle Pathologie und Pharmakologie*, 1962, 243, 546-553.

Determinations in mice of the hexobarbital concentration in the entire body 20 and 60 minutes after injection of 0.14 mg/g i.p. in saline showed that hexobarbital catabolism was still significantly inhibited 5 days after irradiation with 700 r, but was somewhat accelerated 8 and especially 15 days after 400 r as well as 5 days after 700 r if the mice were treated 18 hours earlier with barbital (0.1 mg/g s.c.). The findings probably explain the prolongation of hexobarbital anesthesia following radiation damage.

Pharmakologische Abteilung
Medizinische Forschungsanstalt der
Max Planck Gesellschaft
Göttingen, Germany

27 Praag, H.M. van, & Leijnse, B. The influence of so-called monoamine-oxidase-inhibiting hydrazines on oral loading-tests with serotonin and 5-hydroxy-doleacetic acid. *Psychopharmacologia*, 1962, 3, 202-203.

oral loading tests with 50 mg of the creatinine-sulphate complex of 5HT corresponding to 21.7 mg 5HT and 20 mg 5HIAA were carried out in 4 patients with depression who received isocarboxazid (40 mg per day) and 2 normal subjects who received iproniazid (100 mg/day) before, during and after treatment with the respective MAO inhibitors either alternately or with 1 day intervals. Sjoerdsma's principles were followed, and urinary 5HIAA was determined by Dalglish's technique. Under the influence of isocarboxazid the excretion of 5HIAA after 5HT loading decreased by 35%, and after 5HIAA loading decreased by 42% of the administered dose. With iproniazid these figures were 2% and 39% respectively. No further significant decrease was observed after the 4th day of treatment. Initial values were reestablished 1 week after drug discontinuation. Therefore, MAO inhibitors have a similar and practically synchronous effect on loading tests with 5HIAA and 5HT. As the same mechanism of action appears to be involved, the influence of MAO inhibitors on the 5HT loading test cannot be considered as proof of an inhibition of MAO activity.

Department of Psychiatry
Rijkzigt Hospital
Amsterdam, The Netherlands

28 Salánki, J., & Koschtojanz, Ch. S. Untersuchung der Wirkungen von Serotonin, Tryptamin, Adrenalin, Noradrenalin und LSD auf die Neuroregulation der periodischen Aktivität von Süßwassermuscheln (*Anodonta cygnea*). [The effects of serotonin, tryptamine, epinephrine, levarterenol and lysergide on the neuroregulation of periodic activity in fresh-water mussels (*Anodonta cygnea*).] *Acta Physiologica Academiae Scientiarum Hungaricae*, 1962, 24, 45. [Abstract]

The neural effects of 5HT, tryptamine, LSD and various catecholamines on the

tonus of the closing muscle, and hence on periodic activity, were studied in *A. cygnea* by applying the substances to the cerebral ganglion and recording the activity of the posterior closing muscle. Serotonin, tryptamine, epinephrine and levarterenol were all able to terminate the prolonged tonic contraction of this muscle or to prevent onset of contraction; this was accompanied by a considerable increase in rhythmic activity. LSD produced a gradual but quite marked inhibition of muscle tone. These substances therefore seem to play a significant role in the regulation of the diurnal activity of this mussel.

Institute of Physiology
Medical University of Debrecen
Debrecen, Hungary

2229 Tsukada, Y., & Huszák, I. Enzymic activity related to neural function. I. Effects of environmental complexity and training on brain cholinesterase and brain anatomy in the rat. *Acta Neurologica Scandinavica*, 1962, 38, Suppl. 1, 57-58.

Thirty-one pairs (weaning littermates) of Berkeley S1 male rats were studied under either environmental complexity and training (ENCT) or in isolation (IC). In some cases a triplet was assigned to an intermediate social control (SC) environment. After 80 days the animals' brains were dissected, weighed and analyzed for cholinesterase activity. The ENCT animals showed 2.5% greater acetylcholine activity in both the cortex and the rest of the brain; they also showed a 5.8% greater cerebral cortex weight than IC rats. SC rats showed acetylcholinesterase and brain weight values intermediate between the rats from the other 2 conditions. Over 200 rats of 5 other strains gave similar results. Shorter periods were used in other experiments. Here the differences between ENCT and IC groups were decreased, but still significant. Finally, subjects in other experiments were denucleated at weaning to preclude a visual experience. Here over 400 animals were tested and again environmental stimulation resulted in demonstrable changes in brain chemistry.

ephrine, dopamine, 5HT, metanephrine, normetanephrine, 5HIAA, 3-methoxy-4-hydroxy-mandelic acid. Two solvent systems were used: butanol-pyridine-glacial acetic acid (70:20:10), and isopropanol-ethylacetate-25% ammonia (35:45:20). The colors given by these substances on development with ninhydrin, dichloroquinonechloroimide and diazotized nitroaniline were tabulated. 5-Hydroxyindole acetic acid and 3-methoxy-4-hydroxy-mandelic acid were determined in the urine of normal subjects loaded with these substances and in patients with metastatic carcinoid and pheochromocytoma.

Medizinische Klinik
Friedrich-Alexander-Universität
Erlangen-Nürnberg, Germany

2234 Fossati, P., Caridroit, M., Pruvot, J., Fontan, M., Linquette, M., & Laine, J. Recherches sur l'élimination urinaire de l'acide 5 hydroxy-indol acétique (5HIAA) chez les traumatisés crâniens. [Research on the urinary excretion of 5-hydroxy-indole acetic acid (5HIAA) in cases of cranial trauma.] *Revue Neurologique*, 1962, 107, 659-669.

The quantity of 5HIAA in the 24-hour urine samples was determined for 30 patients suffering from cranio-cerebral and cranial traumas. Excretion became rapidly normalized in cases with hemispheric lesions and remained low for some time in traumas associated with diencephalon-trunk disorders. Excretion was usually normal in patients without severe symptoms. Links between the tryptophane-5HIAA metabolic chain were investigated with ingestions of tryptophane and 5HT, and injections of reserpine. Comparative excretion volumes of 5HIAA, corticosteroids and hydroxycorticoids were also studied. The excretion of 5HIAA seems to be unrelated to medication received. Though results are somewhat inconclusive, it appears that lowered 5HIAA excretion is due to diminution of MAO activity.

Service Neuro-Chirurgicale
Faculté de Médecine de Lille
Lille, France

2235 Cormier, Marcel, & Jouan, Pierre.

Action de la 5-hydroxytryptamine sur la sécrétion in vitro des corticostéroïdes par les capsules surrénales du Rat. [Action of 5-hydroxytryptamine on the in vitro secretion of corticosteroids by rat adrenal glands.] *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences (Paris)*, 1962, 254, 3444-3445.

The adrenal glands of male rats were removed and cut into quarters for incubation with and without 150 µg/100 mg 5HT. Paper chromatography using tetrazolium blue as a developer and UV light was employed for the qualitative estimation of corticosteroids. 5HT caused a clear increase in steroid X₂ and aldosterone; in contrast, steroid X₃, corticosterone and 11-dehydrocorticosterone concentrations were not significantly affected. Serotonin (5HT) has a limited selective action on the genesis of corticosteroids. Quantitatively, the addition of 5HT caused 25-62% increase in corticosteroids.

Faculté de Médecine et de Pharmacie
Université de Rennes
Rennes, France

2236 Put, T.R., & Meduski, J.W. The effect of adrenalectomy on the 5-hydroxytryptamine metabolism in the rat. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 240-256.

Rats were adrenalectomized or sham-operated on; at 3 weeks 90% survived. The metabolism of 5HT was followed through the assay of 5HIAA in 24-hour urine samples and the assay of brain 5HT. There were 5 experimental conditions: untreated, sham-operated, unoperated but given substitution therapy, adrenalectomized, and adrenalectomized and substitution therapy. In substitution experiments the mixture Hydro-Adreson Organon, 25 mg suspended in 1 ml, and DOCA Organon, 5 mg in 1 ml oil were used, i.e., 150 and 350 µg DOCA, and 150 and 350 µg Hydro-Adreson s.c. The observed changes suggest a biphasic type of metabolic response. The 1st post-operative phase (up to 24 hours after surgery) is characterized by the immediate increase of urinary 5HIAA, and unchanged 5HT brain level and impairment

of the "binding-unbinding" and storage mechanisms of 5HT. The 2nd postoperative phase (24 hours after surgery) revealed the impairment of the 5HT binding mechanism and its storage. A scheme is proposed for the mechanism of binding and storage of 5HT.

Department of Neurosurgery
University of Utrecht
Utrecht, The Netherlands

2237 Haefely, W., Thoenen, H., & Hürli-
mann, A. The effect of intraventricular
application of substance P preparations of
different purity. *Medicina Experimentalis*,
1962, 7, 245-249.

Fourteen pentobarbital-anesthetized cats
(cannulated in the right lateral ventricle)
were given intraventricular injections of
substance P in 3 grades of purity: 5, 200
and 2400 μ /mg. Negative results were ob-
tained with highly purified substance P
by intraventricular administration in accord
with previous failure to find specific cen-
tral effects after i.v. injection. Whether
the lack of activity is due to rapid inactiva-
tion or to the failure of substance P to
reach possible specific receptor sites in
the CNS cannot be decided at present.
Central effects of substance P, as reported
by various authors working with crude
preparations, may well be due to other
active principles present in extracts. The
crude extract had an initial stimulant effect
on the CNS followed by a depression, which
is also caused by equivalent amounts of
ammonium sulphate (the protein precipit-
ating agent).

Department of Experimental Medicine
F. Hoffmann-La Roche & Co., Ltd.
Basel, Switzerland

2238 Panagopoulos, K., Matsopoulos, K.,
Damigos, E., Kallistratos, G., Vavougi-
os, J., Gregoriades, G., & Pfau, A. Biological

acetylation. 7th Communication. The dis-
turbances in the mechanism of in vivo
acetylation and the metabolism of pyruvic
and citric acids after administration of
barbiturates. *Medicina Experimentalis*,
1962, 6, 237-244.

Healthy volunteers and patients of both
sexes maintained on a standard diet, were
studied in relation to the biosynthesis of
pyruvic and citric acids and acetylation.
Normal values for blood and urine were
determined in the 37 subjects before the
administration of barbiturates and 12 mg
per kg PABA. Four groups were given
barbiturates p.o. as follows: 75 and 150 mg
per kg phenobarbital, 75 and 150 mg/kg
pentobarbital, 50 and 100 mg/kg barbita-
l and 75 and 150 mg/kg pentobarbital. Bar-
biturates prevent the formation of pyruvic
acid and decrease citric acid concentra-
tions; they also hinder the in vivo acetyla-
tion of PABA. Administration of sodium
pyruvate concomitantly with barbiturate
normalizes pyruvic and citric acid meta-
bolism but not the in vivo acetylation.
Aside from the role of pyruvic acid as a
limiting factor, other possibilities involve
in the decrease of citric acid concentration
may be: the reduction of pyruvic dehydro-
genase, acceleration of oxalacetic acid syn-
thesis and the inactivation of the corres-
ponding enzyme, through the barbiturates
which may hinder the condensation of acetyl
CoA with oxalacetic acid, necessary for
citric acid production.

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See also 2023, 2172, 2200, 2204

ABBREVIATIONS

KG	α -ketoglutarate	F	Fahrenheit scale
ACL	Zuckerman's Affect Adjustive Check List	FDA	Federal Drug Administration
		FFA	free fatty acid
ATH	adrenocorticotrophic hormone		
lib.	free choice	g	gram
ADP	adenosinediphosphate	GABA	γ -aminobutyric acid
M	morning	GABOB	γ -amino- β -hydroxybutyric acid
AMA	American Medical Association		
t.	Article	HD	hypnotic dose
ATP	adenosinetriphosphate	5HIAA	5-hydroxyindoleacetic acid
		5HT	5-hydroxytryptamine
		5HTP	5-hydroxytryptophane
AI	Bell Adjustment Inventory		
AL	British antiLewisite	i.a.	intrarterial
AS	benzyl analogue of serotonin	ibid.	in the same place
d.	twice a day	i.e.	that is
DL	bromolysergic acid diethylamide	i.m.	intramuscular
UN	blood urea nitrogen	IMPS	Lorr's Inpatient Multidimensional Psychiatric Scale
		i.p.	intraperitoneal
	Celsius scale	IPAT	Cattell's Institute for Personality and Ability Testing Anxiety Scale
	about		
AR	conditioned avoidance response		
CS	chronic brain syndrome		
	cubic centimeter	IQ	intelligence quotient
OC	Communicable Disease Center	IU	international unit
2	square centimeter	i.v.	intravenous
3	cubic centimeter		
R.S.	Centre National de la Recherche Scientifique	kg	kilogram
IS	central nervous system	K _i	Michaelis constant for an inhibitor
DMT	catechol-o-methyl transferase	K _m	Michaelis constant for a substrate
m	counts per minute		
s	counts per second		
R	conditioned reflex (response)	lbs	pounds
	conditioned stimulus	LD	lethal dose
TD	climbing time delay	LSD	lysergide
OT	dichlorodiphenyl trichlorethane	μ	micron
IA	deoxyribonucleic acid	μ c	microcurie
DPA	3, 4-dihydroxy-phenylalanine	μ g	microgram
PN	diphosphopyridinenucleotide	μ l	microliter
PNH	reduced diphosphopyridinenucleotide	μ M	micromolar
		m	meter
		M	molar
EG	electrocardiogram	ma.	millamperes
ET	electroconvulsive therapy	MACC	Motility Affect Cooperation Communication
.	editor		
O	effective dose	MAO	monoamine oxidase
OTA	ethylenediaminetetraacetic acid	MAS	Taylor Manifest Anxiety Scale
EG	electroencephalogram	meq	milliequivalents
g.	for example	ml	milliliter
RG	electroretinogram	mm	millimicron
T	electroshock treatment	mm	millimeter
al.	and others	mM	millimolar
c.	and so forth	mm ²	square millimeter

MMPI	Minnesota Multiphasic Personality Inventory	SGPT	serum glutamic pyruvic trans-aminase
MPI	Maudsley Personality Inventory	sic	exactly as found
MSRPP	Multidimensional Scale for Rating Psychiatric Patients	SRA	Science Research Associates
		SSAI	Springfield Symptom and Adjustment Index
N	normal	Suppl.	supplement
NEFA	nonesterified fatty acid		
NIH	National Institutes of Health	TAT	Thematic Apperception Test
NIMH	National Institute of Mental Health	TCA	trichloroacetic acid
		TD	toxic dose
NINDB	National Institute of Neurological Diseases and Blindness	TH	thyroid hormone
		t.i.d.	thrice a day
p	probability	TPN	triphosphopyridinenucleotide
PABA	para-aminobenzoic acid	TPNH	reduced triphosphopyridinenucleotide
PAH	para-aminohippuric acid	TSH	thyroid-stimulating hormone
PBI	protein-bound iodine		
pH	negative logarithm of hydrogen ion concentration	U	unit
PM	afternoon and evening	UR	unconditioned response
p.o.	by mouth	US	unconditioned stimulus
ppm	parts per million	USAF	United States Air Force
PRP	Psychotic Reaction Profile	USDHEW	United States Department of Health, Education, and Welfare
q.i.d.	four times a day	USP	United States Pharmacopoeia
refs.	references	USPHS	United States Public Health Service
Rf	ratio of the distance of dissolved substance to solvent distance	UV	ultraviolet
RNA	ribonucleic acid	VA	Veterans Administration
ru	rat unit	viz.	namely
s.c.	subcutaneous	WAIS	Wechsler Adult Intelligence Scale
S.D.	standard deviation	WHO	World Health Organization
SGOT	serum glutamic oxaloacetic transaminase	WPRS	Wechsler Psychiatric Rating Scale

ERRATA

The following corrections should be noted:

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Wada, Juhn A. Behavioral and electrophysiological effects of intraventricular injection of bulbocapnine and other substances in freely moving monkeys. In: Sankar, D.V. Siva [Ed.] Some Biological Aspects of Schizophrenic Behavior. *Annals of the New York Academy of Sciences*, 1962, 96, Art. 1, 7-250.

Segal, Mark, & Denau, G.A. Brain levels of epinephrine (E), norepinephrine (N), dopamine (D) and 5-HT during administration and withdrawal of morphine

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978 Funderburk, William H., Finger, Kenneth F., Drakontides, Anna B., & Schneider, Jurg A. EEG and biochemical findings with MAO inhibitors. In: Sankar, D.V. Siva [Ed.] Some Biological Aspects of Schizophrenic Behavior. *Annals of the New York Academy of Sciences*, 1962, 96, Art. 1, 289-302.

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1014 Yasuda, Manabu. Effect of reserpine on febrile responses induced by pyrogenic substances. *Japanese Journal of Pharmacology*, 1962, 11, 114-125.

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From 5 to 20 mg/kg i.p., the action of chlordiazepoxide (methaminodiazepoxide) on the aggressive behavior of male rats toward mice was practically negligible. Starting with 30-35 mg/kg, interspecific aggressiveness was abolished in most rats,

the criterion being the number of rats which killed mice. Ataxia was prevalent at this dosage level, and transitory suppression of aggressiveness seemed to be the consequence of side effects, particularly the ataxia, and not due to a selective action of the drug. Chlordiazepoxide had properties resembling those of meprobamate, but seemed about 5 times more active.

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Serum taken from hospitalized male schizophrenics, aged 29-62 years, was injected i.v. into rabbits, of which 2 out of 6 received 5 ml of normal serum and 2 received no injection. Animals were sacrificed after 16 hours, and the hypothalamus, the remainder of the brain stem and the cerebral cortex were analyzed for 3 catecholamines: epinephrine, levarterenol and dopamine. Epinephrine and levarterenol were estimated by the trihydroxyindole method and dopamine by a combination of the trihydroxyindole and ethylenediamine method. In contrast to the results of Minz and Waleszek (1958), no significant differences were produced by normal or schizophrenic sera.

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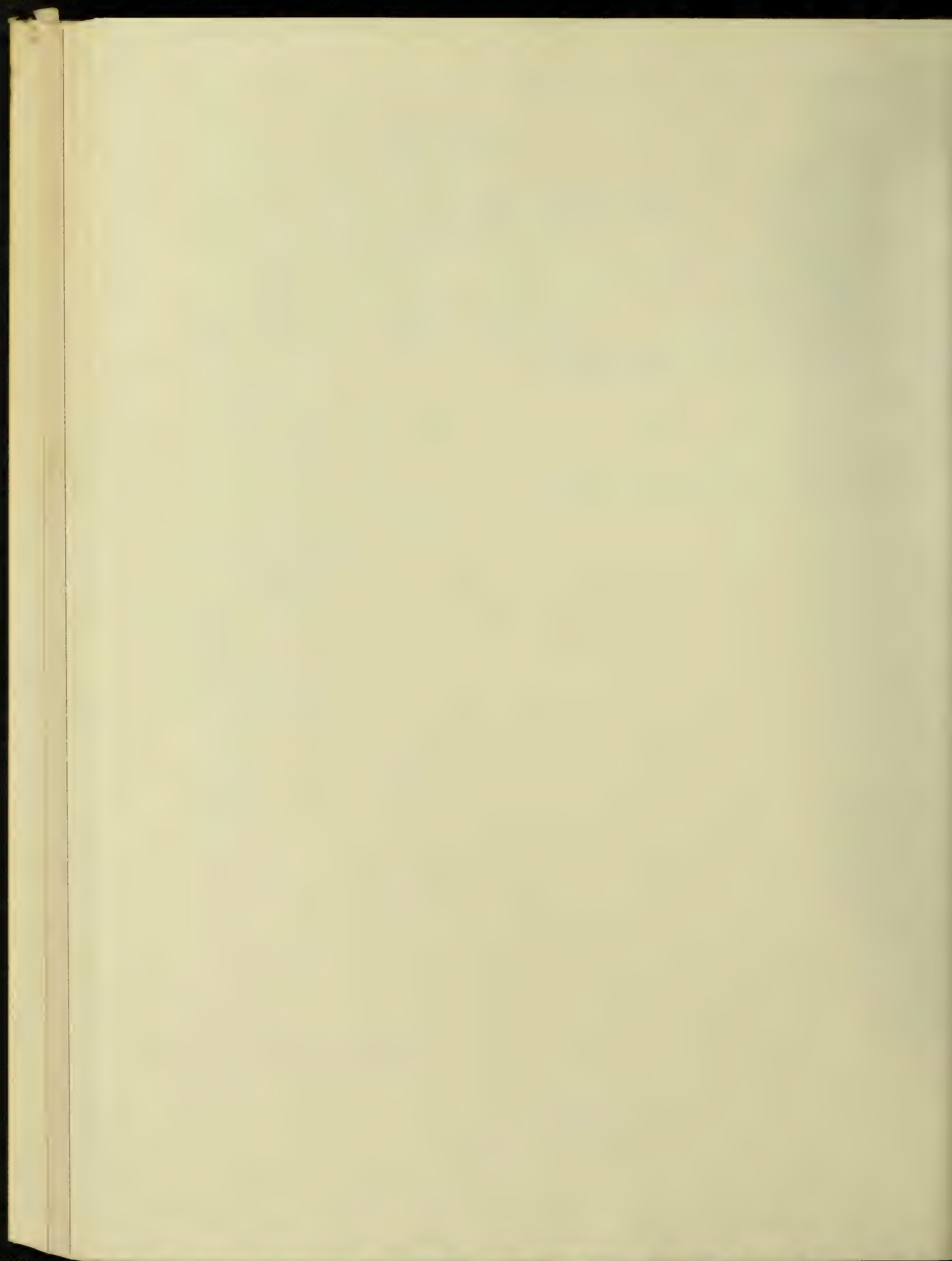
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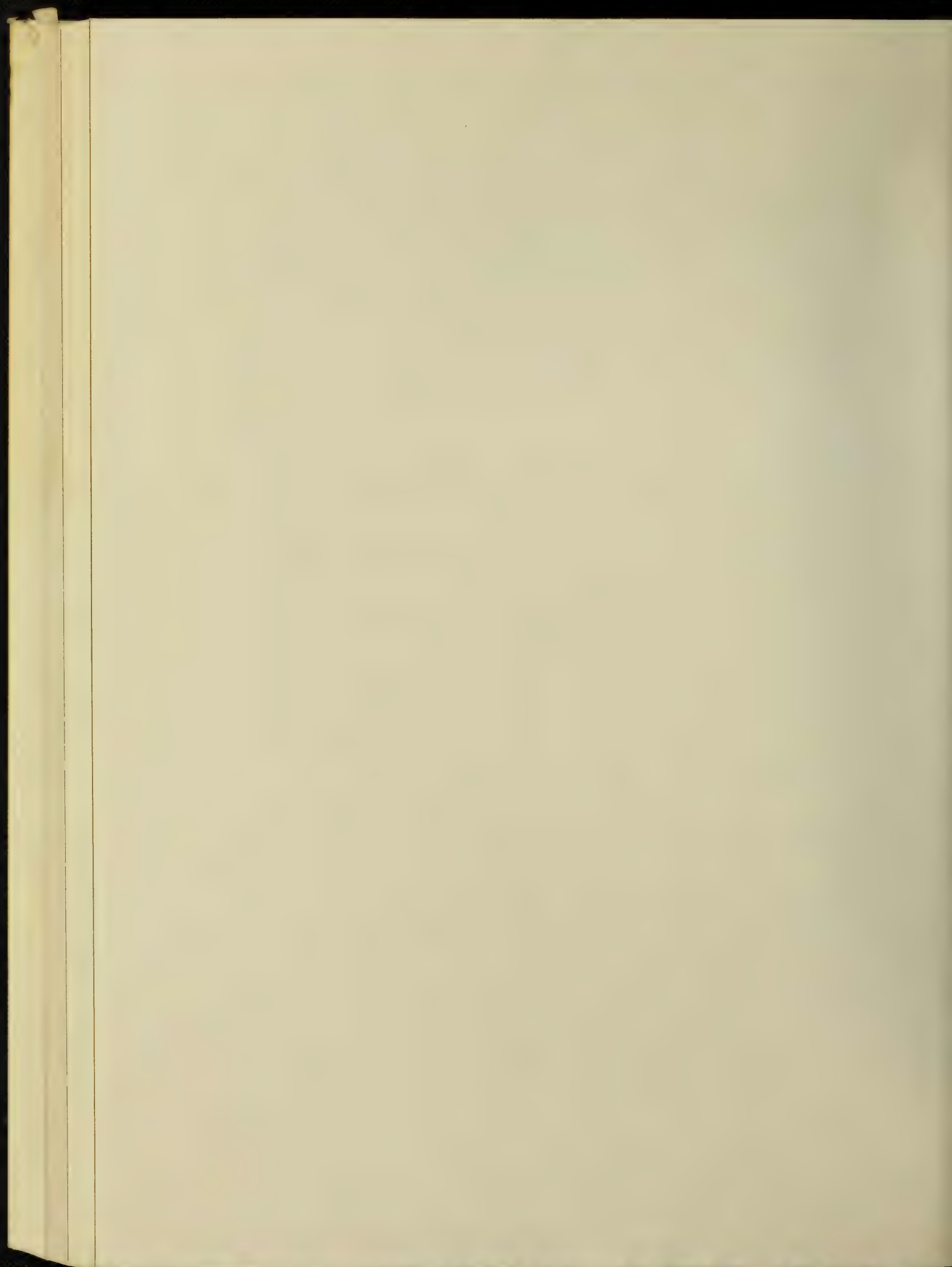
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U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
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National Institutes of Health
National Institute of Mental Health
Bethesda 14, Maryland

PSYCHOPHARMACOLOGY ABSTRACTS

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REVIEWS, SUMMARIES, BIBLIOGRAPHIES,
GENERAL ARTICLES AND BOOKS

2239 Huxley, Julian. Psychometabolism. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S1-S14.

Schizophrenia is balanced psychometabolic morphism. About 19% of all people are schizophrenic; the disease appears to have a strong genetic basis and genetic theory indicates that such a clearly disadvantageous entity could not persist in a population unless it is balanced by a compensatory advantage. Biochemical studies indicate that adrenochrome or adrenolutin constitutes the genetically determined basis for schizophrenia. Perceptual anomalies tend to accompany biochemical abnormalities. Minimal doses of hallucinogens like mescaline, LSD and psilocybin exert similar dislocating effects on perception, which effects resemble acute transient schizophrenia. Work must be undertaken to determine whether psychotomimetics modify or enhance dreaming. Significant contributions to psychiatry and psychology include experimental work on mother surrogates, taste perception, pain sensitivity, manipulative behavior, the genetic basis for species awareness and the establishment of intraspecific emotional bonds. (40 refs.)

31 Pond Street
Hampstead N.W. 3
London, Great Britain

2240 Leconte, Maurice. Etude clinique et traitement du mutisme en médecine psychiatrique. [Clinical study and treatment of mutism in psychiatry.] *Annales Médico-Psychologiques*, 1962, 120, 2, 886-908.

Mutism in psychiatric patients may be voluntary, as in chronic delirium, (in which it may be motivated, or occur as an act of defiance, or in obedience to hallucinatory voices, or the result of excitational, discordant, or oligophrenic syndromes), or it may be involuntary as in hysterical, aphonic and aphasic syndromes. It tends to be complete in the melancholic, confusional, and catatonic stupor syndromes. It occurs in partial forms in melancholic, delirious, demential, oligophrenic, obsessional, and psychic-disequilibrium syndromes. Treatment should be both etiologic and symptomatic. Pentetrazol is indicated in post-confusional mutisms, in apathy, but

may sometimes result in anxiety states. ECT and various narco-analeptic agents are often useful. Methamphetamine at 30 mg i.v. can be used for the exploration of mutism, since it augments the patient's speech and induces emotional discharge, but frequently the contraindications hypertension, arteriosclerosis and exophthalmic goiter are noted. Psychotherapy is helpful but more important in prophylaxis than in therapy. Further, a single case is presented in which chlorpromazine proved of benefit. In children, the drawing-test methods, accompanied by empathy and comprehension are also useful. (38 refs.)

Centre Psychiatrique Sainte-Anne
Paris, France

2241 Jermulowiecz, Z.W., & Turnau, Mag. A. Control and treatment of drug addicts in Israel. *Bulletin on Narcotics*, 1962, 14, 11-18.

With the establishment of the State of Israel in 1948 and mass immigration from the Arab countries, the problem of drug addiction assumed serious proportions in Israel. Lack of hospital facilities delayed treatment and in 1952 the Ministry of Health began to allocate drugs to addicts until they could be hospitalized. Finally, an institutional program was created. Thus far, 274 addicts have been hospitalized. Addicts are initially kept in a closed ward with psychotic patients and then transferred to a special ward. Addicts prefer the special ward and are highly motivated to recover rapidly. Success in initial weaning is largely attributed to chlorpromazine (initially 150 mg, then 400-500 mg/day). Group as well as individual psychotherapy is also of value. The most toxic drug among addicts is pethidine, which leads to epileptic seizures after use for 1-1½ years. Illiterates who were opium addicts since adolescence and those over 45 years of age who have never worked creatively are the most difficult to cure. At present, it is estimated that those who fail to relapse constitute 2-3% and prevention of addiction is far more successful than cure. (No refs.)

Government Hospital for Mental Patients
Bat-Yam, Israel

Reviews
Abstracts 2242-2245

2242 Blazek, J., Spinkova, V., & Stejskal, Z. Analytik der Phenothiazinderivate. Übersicht. [Analysis of phenothiazine derivatives. A review.] *Pharmazie*, 1962, 17, 497-514.

Analytical methods for the determination of phenothiazine derivatives are presented. Three tables are given listing chemical names, formulas, generic names, and therapeutic use of phenothiazine derivatives not substituted in the ring, those substituted in the ring, and those not substituted at the nitrogen. An extensive list of synonyms for the various phenothiazine derivatives is also given. (218 refs.)

Staatliches Institut für Arzneimittel-
kontrolle Prag
Prague, Czechoslovakia

2243 Linke, H. Möglichkeiten und Probleme der Psychopharmakotherapie im höheren Lebensalter. [Possibilities and problems of psychopharmacologic therapy in advanced age.] *Zeitschrift für Ärztliche Fortbildung*, 1962, 15, 805-811.

Physiologic aging, frequently accompanied by psychological phenomena and emotional disturbances (due to arteriosclerotic and other organic changes) is expounded. Psychopharmacologic agents, often in combination with a sedative or a circulatory stimulant, play a vital role in the attempt to brighten the prolonged evening of life. Four most frequently occurring geriatric problems are: the manifold symptoms presented by retardation of psycho-physical agility; various forms of geriatric insomnia; treatment of psychomotor agitation and confusion, and treatment of depressive states of anxiety and mood disturbance. Successful treatment depends upon use of the proper psychotropic agents, good psychotherapeutic guidance and an environment free of stress and conflict. (No refs.)

Medizinische Klinik
Medizinische Akademie
Magdeburg, Germany

2244 Himwich, H.E., Morillo, Arturo, & Steiner, William G. Drugs affecting rhin-

encephalic structures. *Journal of Neuro-psychiatry*, 3, Suppl. 1, S15-S26.

With regard to the effects of drugs on the amygdala and hippocampus, meprobamate and pentobarbital decrease the sensitivity of rhinencephalic structures and EEG tracings show that after-discharges, evoked by stimulation, are either shortened or prevented by these drugs. The antidepressant (imipramine, demethylimipramine, amitriptyline and chlorprothixene) increases the sensitivity of rhinencephalic structures. This enhanced sensitivity is evidenced by spontaneous positive spiking occurring in the amygdala and various other brain areas except for the neocortex. Chlordiazepoxide and diazepam depressed activity in the amygdala, but stimulated it in the hippocampus. Perusal of the literature yielded work on the reverberating circuit of Papez, Cannon's theory of emergency sympathetic nervous system mobilization and Bard's hypothalamic stress theories. (29 refs.)

Thudichum Psychiatric Research Laboratory
Galesburg State Research Hospital
Galesburg, Ill.

2245 Stempel, Edward. The impetus of thalidomide on drug legislation and regulation. *American Journal of Pharmacy*, 1962, 134, 355-364.

The thalidomide tragedy precipitated enactment of a welter of legislation designed to increase the stringency of federal law regulating all facets of the U.S. pharmaceutical industry. Such regulations may prove excessive, but Americans are bound to feel more secure with improved standards of testing, sterner controls on licensing, more precise labeling and the power of the Government to immediately remove a drug from the market whenever such action is deemed necessary. (45 refs.)

Department of Pharmacy
Brooklyn College of Pharmacy
Brooklyn, N.Y.

2246 Schain, Richard J. Actions of pharmacologically active substances in cerebro-

spinal fluid upon the central nervous system. *World Neurology*, 1962, 3, 706-714.

Injections of various pharmacologically active substances (acetylcholine and cholinesterase inhibitors, 5HT, catecholamines, curare, tryptamine, potassium and calcium salts, CSF, LSD, morphine, reserpine, mescaline and chlorpromazine) into the lateral ventricle of conscious cats produces characteristic behavioral and neurologic effects, predominantly convulsions, muscular hypotonia, ataxia and stuporous states. These studies indicated that the periventricular region is an area of high pharmacologic sensitivity. Minute CSF drug concentrations produce profound effects on the CNS. A bioassay preparation may be used as an excitable organ in order to reflect the biological properties of CSF and as a means of measuring substances present in subthreshold concentrations. Acetylcholine is present in CSF and perfusates of the ventricular system. Specialized chemoreceptors in the walls of the 4th ventricle may provide the means by which pharmacologically active substances in CSF affect the CNS. (62 refs.)

Section of Neurology
Yale University School of Medicine
New Haven, Conn.

2247 *Lancet*. The premature persuaders. *Lancet*, 1962, No. 7222, 198-199. [Editorial]

All physicians in the United Kingdom have recently received a letter warning of the possible untoward effects of thalidomide. In New York, similar warning letters have preceded withdrawal of 7 drugs from the market (triparanol, zoxazolamine, erythromycin, triacetyloleandomycin, furaltadone, diazthazanine and amphenidone). A new drug should never be brought into general use unless it is clearly more effective than existing remedies. Drug efficacy can be determined only by properly planned controlled therapeutic trials. A feasible system should be inaugurated whereby clinical trials are performed by reliable groups of clinicians dealing primarily with such endeavors. (No refs.)

7, Adam Street, Adelphi
London W.C. 2, Great Britain

2248 Winkler, K., & Gröger, D. Neuere Arbeiten zur Biosynthese der Mutterkornalkaloide. [Recent literature on the biosynthesis of ergot alkaloids]. *Pharmazie*, 1962, 17, 658-670.

The review deals with papers published since 1950. Extensive experiments are discussed which, with the aid of isotopic labeling, have shown the incorporation of tryptophan and of a C5 derivative of "mevalonic acid" into ergot alkaloids, including LSD. Anthranilic acid and/or indole can be used as precursors during the biosynthesis of tryptophan. The transformation of certain alkaloids by chemical means is briefly outlined. Numerous formulas explain hypothetical and proven pathways. (98 refs.)

Pharmakognostisches Institut
der Martin Luther Universität
Berlin, Germany

2249 Dunlop, Edwin. The neurotic feeling of inferiority. *Journal of Neuropsychiatry*, 1962, 3, S79-S82.

Patients with reactive depression complicated by anxiety and depersonalization exhibiting hysterical behavior will often respond to antidepressant drugs, but about 75% require some additional medication, such as a phenothiazine, meprobamate or chlordiazepoxide, accompanied by nocturnal sedation. The necessary pot pourri of drugs makes delineation of drug-induced side effects difficult. Patients with classical neurotic depression respond very well to treatment with diazepam. After acute withdrawal therapy, alcoholics respond well to 30-40 mg of diazepam per day. Acute schizoaffective disorders show satisfactory improvement with diazepam but no convincing results have been obtained in acute paranoia or chronic regressed schizophrenia. (No refs.)

Fuller Memorial Sanitarium
South Attleboro, Mass.

2250 Branch, C.H. Hardin, Himwich, Harold, Feldman, Robert S., McConnell, James, & Shagass, Charles. Panel discussion. *Journal of Neuropsychiatry*, 1962, 3, S59-S61. [Discussion]

A panel discussion encompasses the following topics: comparison of averaging techniques with examination of raw EEG data, present evidence for MAO inhibition as an important factor in relieving depression, severe depression experienced 4-5 hours after an initial dose of meprobamate, interaction effects of psychoactive drugs, results obtained with excessive doses of pentobarbital, antidepressants and chlordiazepoxide, administration of chlordiazepoxide during conflict, conditioning in worms, biochemical fractionation of trained worms, the application of worm conditioning to the mentally retarded, rate of regeneration and cannibalization in worms, potential corroboration of the theory that acquired traits can be transmitted genetically, relation between breast feeding and intelligence, non-segmented worms and categorization of the phenothiazines. (No refs.)

[No address]

2251 Callaway, Enoch, Feldman, Paul, Towler, Martin L., Gibbs, Frederic A., Detre, Thomas P., Collard, J., Katz, Robert & Shea, Paul A. Panel discussion. *Journal of Neuropsychiatry*, 1962, 3, S83-S90. [Discussion]

An extensive panel discussion provided elaboration on the following topics: the use of diazepam in adolescents, EEG changes with various phenothiazines, fast EEG activity secondary to alcoholism, transient drowsiness following diazepam ingestion, the anticonvulsant action of psychotropic drugs, the relationship of fast EEG activity and withdrawal seizures, relief of neuromuscular symptoms with diazepam or chlordiazepoxide, maintenance dosage in responsive depressed patients, large doses as a means of obviating the overstimulating effect of 2.5-5 mg doses of diazepam, muscle relaxant properties of diazepam, duration of diazepam therapy in depression to determine therapeutic efficacy, diazepam as an analgesic, incidence of suicide in relation to diazepam and chlordiazepoxide, alterations in dreams during diazepam therapy, the definite potentiating effects of diazepam on alcohol, automobiles and diazepam, and diazepam as an effective sedative. (No refs.)

[No address]

2252 Collard, J. Drug responses in different ethnic groups. *Journal of Neuropsychiatry*, 1962, 3, S114-S121.

In conjunction with a survey of the literature on ethnic response, the following parameters are examined in several ethnic groups: reactive modes to various stimuli and determining factors, the liminal stimulus (particularly drug dosages required to reach the therapeutic threshold) and genetic determination (pharmacogenetics). With regard to reactive modes, the following topics are studied: reactions to conflicts, group pressure, psychotic processes and psychotropic therapies. Comparison of liminal stimuli revealed that considerable variations were observed between the average American and European doses of neuroleptic drugs. Pharmacogenetic studies demonstrate the importance of genetic determinism in animals and human subjects with relation to drug response. In an experimental comparison between an American and a European group of psychotics in response to haloperidol, the mean threshold of pharmacologic and therapeutic reactivity of the American group was 10 times greater than the corresponding European threshold. Not a single American patient showed a threshold lower than the highest European threshold. Morbidity profiles and ethnosociocultural structures are evaluated for the groups in question. Ethnologic reactivity must be determined by ecology and genetics. (25 refs.)

Psychiatric Clinic
University of Liège
Liège, Belgium

2253 Kahn, J.P., Sargant, William, Masserman, Jules H., & Ruesch, Jurgen. Panel discussion. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S130-S132. [Discussion]

A panel discussion included the following topics: the relationship between cessation of medication and relapse, maximal dosage range of drugs commonly used in acute psychoses, the role of ECT, the advisability of having 1 physician administer psychotherapy and ECT, introduction of person-centered programs into institutions, time comparisons between neurotic monkeys that were treated successfully with drugs and

Attempts to deneuroticize neurotic monkeys without benefit of drugs (Masserman 1962) and maximal dosages of chlordiazepoxide combined with MAO inhibitors in atypical depressions and anxiety states. (No refs.)

[No address]

2254 Finley, Knox H., Merlis, Sidney, Wilkin, Morris I., Proctor, Richard, & Dunlop, Edwin. Panel discussion. *Journal of Neuropsychiatry*, 1962, 3, Suppl. 1, S155-S156. [Discussion]

A discussion of merits of chlordiazepoxide and diazepam encompasses the following topics: the self-limiting nature of depression, possible potentiation of sedatives and hypnotics by diazepam, the overall efficacy of psychotropic drugs, the nature of modified ECT, diazepam in hypomanic states and clinical differences, diagnostic indications, and differential advantages of chlordiazepoxide and diazepam. (No refs.)

[No address]

2255 Guy's Hospital Gazette. Research at Guy's. *Pharmacology*. *Guy's Hospital Gazette*, 1962, 76, 507-512. [Editorial]

Five main lines of research being carried on are reviewed. The 1st, a study of the effects of drugs on the endocrine system, was undertaken when it was found that 5HT and MAO inhibitors have striking effects in pregnancy thought to be caused by 2 main mechanisms: interference with the hormonal action necessary for maintenance of gestation and interference with the placental function. In connection with this research, the effects of exogenous ACTH was investigated in both mature and immature mice and experiments with rabbits are also described. Other areas of research include: the effect of drugs on intestinal absorption; the chemotherapy and immunology of mycobacterial diseases, the normal physiological control of the ileocolic sphincter and the effect of drugs on this part of the intestine, and investigation of the mechanism of inflammation, etc. (No refs.)

Guy's Hospital
London, Great Britain

2256 Norton, Alan. The chemotherapy of the major psychoses. *Guy's Hospital Gazette*, 1962, 76, 172-176.

The use of major tranquilizers (reserpine, the phenothiazines and the piperazine phenothiazines), the thymoleptics (imipramine and amitriptyline), the MAO inhibitors and psychotomimetic drugs, in treating schizophrenia, manic and depressive psychoses and some kinds of nonpsychotic depression is discussed. (No refs.)

[No address]

2257 Mandel, P., & Weill, J.D. Nucléotides du système nerveux central. [Nucleotides of the central nervous system.] *Journal de Physiologie*, 1962, 54, 199-267.

The constitution of nucleotides, methods of separation and identification of free nucleotides, their biosynthesis, their role in enzymatic mechanisms, and their physiological chemistry are reviewed. In relation to nucleotide in vitro physiological chemistry, energy metabolism, ion exchange, the relationship between acetylcholine and free nucleotides and the effects of electric stimulation are detailed. In vivo studies are reviewed in regard to the generation of nucleotides throughout growth, the reformation of free nucleotides, the effect of cerebral hyperactivity, convulsant agents and electroshock, hypoxia, anoxia, anesthetics and various pharmacologic agents. Among the latter chlorpromazine and "promazine" are noted as influencing the in vivo synthesis of DPN (Burton et al. 1958), but evidence is insufficient for the formulation of a valid hypothesis concerning phenothiazine mechanism of action. (533 refs.)

Institut de Chimie Biologique
Faculté de Médecine
Strasbourg, France

2258 DeProspero, Chris J. News and notes. *American Journal of Mental Deficiency*, 1962, 67, 133-136.

The Guthrie test (which uses a few drops of blood from a newborn's heel to detect phenylketonuria) provides the basis for

inauguration of a new national program which may prevent mental retardation resulting from phenylketonuria and other inborn errors of metabolism. The Guthrie test will be utilized to screen some 400,000 newborn babies as of July 1, 1963 in cooperation with various health departments and hospitals. Once phenylketonuria is diagnosed, special diet arrangements can be instituted which will preclude development of the disease with its concomitant irreparable mental retardation. During 1960, the ferric chloride urine test detected more than 25 infants with phenylketonuria. Dietary treatment was promptly instituted to prevent mental retardation. (No refs.)

[No address]

2259 Peters, Rudolph A. Seminar on the physiology and biochemistry of disturbed brain function: Introductory statement. *Journal of Neuropsychiatry*, 1962, 4, 105-106.

Convulsions may be produced in pigeons by disrupting the Krebs' cycle at any number of points: thiamine deficiency or BAL prevent the oxidation of pyruvate to acetyl co-A, fluorocitrate inhibits triosephosphate dehydrogenase and lewisite inhibits the oxidative decarboxylation of α -ketoglutarate. In addition, injection of Cu^{++} into the subarachnoid space in pigeons rapidly produces convulsions and death by irreversibly inhibiting some component of pyruvic dehydrogenase. Irreversible convulsions follow injection of fluorocitrate into the subarachnoid space in pigeons. Convulsions induced by thiamine deficiency stop within 30 minutes if thiamine is injected into the brain. Internal changes in the nerve cell must therefore modify all subtle pharmacological reactions. (No refs.)

Department of Biochemistry
University of Cambridge
Cambridge, Great Britain

2260 Hagen, Paul B. Some current ideas on the biosynthesis and storage of simple amines and some consideration of their relationship to central nervous function. *Journal of Neuropsychiatry*, 1962, 4, 107-112.

Germane to CNS localization of simple amines, most levarterenol is located in the hypothalamus and most dopamine may be found in the basal ganglia. Levarterenol and dopamine are catecholamines of adrenergic nerves along with traces of epinephrine. Whether brain catecholamines are present in specialized amine storage cells or in neurones or glial cells remains a hypothetical question. Dopamine is in solution in the fluid cytoplasm, but epinephrine and levarterenol are located within special cytoplasmic storage granules as the adenine nucleotide salts. In mammals, 5HT is found principally in the argentaffin cells of the alimentary canal, but in brain tissue it is stored in granules of lower specific gravity than mitochondria. Acetylcholine is stored in brain vesicles. The function of GABA remains unknown at present, as does the function of taurine. (24 refs.)

Department of Biochemistry
University of Manitoba
Winnipeg, Manitoba
Canada

2261 Pletscher, A. Basic aspects of psychotropic drug action. *American Journal of Mental Deficiency*, 1962, 67, 238-244.

Rauwolfia alkaloids with sedative action (e.g. reserpine) and benzoquinolizine derivatives with sedative action (e.g., tetrabenazine) decrease the storage capacity for monoamines like 5HT, levarterenol and dopamine. Administration of α -methyldopa or 2-methyl 5HTP results in a fall of brain 5HT, levarterenol and dopamine through blocking monoamine formation by preventing decarboxylation of monoamine precursors. Irreversible (long acting) MAO inhibitors include hydrazine derivatives like iproniazid, isocarboxazid, pheniprazine, phenelzine, tranlylcypromine, etc. Hormone derivatives like harmine and harmaline are short acting or reversible MAO inhibitors. Inhibition of MAO degradation by these drugs increases the brain content of various endogenous monoamines. Certain phenothiazines (chlorpromazine) and thioxanthenes (chlorprothixene) inhibit monoamine penetration through biological membranes. Thymoleptics like imipramine and amitriptyline may exert their influence by increasing the monoamine sensitivity of CNS receptor sites.

Medical Research Department
F. Hoffmann-La Roche and Co., Ltd.
Basel, Switzerland

2262 Schulte, W. Psychotherapeutische Bemühungen bei der Melancholie. [Psychotherapy of melancholy.] Deutsches Medizinische Wochenschrift, 1962, 81, 2225-2231.

A distinction must be drawn between depressives and melancholics. The latter do not feel "sad" but rather "indifferent", "empty", "lifeless", etc. Indifference expresses itself in a dull personality and carelessness grooming. Contact and therapy are difficult because the physician is mistrusted and considered incapable of understanding the uniqueness of the patient's condition. During the freer intervals the patient may be brought to accept the melancholic phase as part of his life and to place confidence in the physician, who must also subsequently be always available to fortify the patient against his fear of reentering the external world. Psychotropic drugs are useful but doses must be carefully watched or the patient may regress. (No refs.)

Universitäts Nervenlinik
Osianderstrasse 22
Tübingen, Germany

2263 Beskin, Harry. Psychiatric inpatient treatment of adolescents. A review of clinical experience. Comprehensive Psychiatry, 1962, 3, 354-369.

This review of the residential psychiatric care of adolescents includes historical background, nonhospital facilities, psychiatric facilities, adolescent-adult wards versus all-adolescent wards, problems in controlling aggressive, destructive and acting-out behavior, and follow-up results. Admixture of adolescent and adult patients seemed helpful although there were some differences of opinion. The dearth of systematic investigation into the problem of treating adolescents in psychiatric hospitals was noted. Drug therapy is mentioned (i.e., phenothiazines) but no details were given. (51 refs.)

Massachusetts Mental Health Center
Boston, Mass.

2264 Weingärtner, L. Zur medikamentösen Therapie Neu- und Frühgeborener [Drug therapy of newborn and premature infants] Zeitschrift für Ärztliche Fortbildung, 1962, 17, 969-972.

Newborn and premature infants require often greatly reduced dosages of drugs, unrelated to body weight. Thirteen potentially dangerous drugs, hormones and vitamins are listed, including opiates, atropine, barbiturates and phenothiazines. Metabolic processes required for excretion or detoxication are not fully developed in these infants, and may easily be damaged by drugs. The role of enzymes and the significance of enzymatic defects are discussed in connection with certain hereditary diseases. (No refs.)

Universitäts-Kinderklinik
der Martin Luther-Universität
Halle-Wittenberg, Germany

2265 Chatagnon, C., & Chatagnon, P. A. Les drogues en gériatrie et en gériatrie-psychiatrique. [Drugs in geriatrics and psychiatric geriatrics.] Annales Médico-Psychologiques, 1962, 120, 2, 231-242.

Utilization of hypocholesterolemic, anticoagulants, vasodilators, and rauwolfia derivatives in geriatrics necessitates great attention to dosage requirements. Hormone treatments and vitamin therapy are frequently useful, particularly in cases of senile osteoporosis. A large number of stimulants has been in vogue and on occasion, favorable results have been obtained when placental or amniotic lyophilized extracts were used on depressive senile patients. Tolerance to various sedatives and hypnotics is lower in older persons, and patients must be carefully observed for certain secondary symptoms such as Cheyne-Stokes respiration or morphine-induced depression of the respiratory center. Psychoactive drugs, particularly tranquilizers and ataractics are more dangerous to older persons than is commonly realized, and dosages should be minimal. Little is known of their mechanisms of action or biochemical effects. Chlorpromazine is excreted, not stored within the body; its transitory

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biochemical effects include higher erythrocyte sedimentation rate with concomitant variation of blood viscosity, lower fibrinemia and potassiemia. Large doses over a long period of time will cause slight weight loss and possible convulsions. (No refs.)

Hôpital de Maison-Blanche
Neuilly-sur-Marne, France

2266 Berger, F.M. The treatment of anxiety. A critical review. *Journal of Neuropsychiatry*, 1962, 4, 98-103.

Anxiety is an organic or functional disturbance of the brain rather than the mind since the mind is merely a manifestation of brain activity. Considerable evidence contradicts Freudian and Pavlovian concepts of anxiety. Psychologically, anxiety is manifested as a unitary factor which is neither a primary drive nor related to the general drive level. Deleterious anxiety may be ameliorated by 2 basic pharmacological drugs: meprobamate and chlorpromazine. Meprobamate, the drug of choice appears to act directly on anxiety, while chlorpromazine specifically counteracts hallucinations. (9 refs.)

Wallace Laboratories
Cranbury, N.J.

2267 LaVerne, Albert A. Compendium of neuropsychopharmacology. Preparations used in treatment of alcoholism. *Journal of Neuropsychiatry*, 1962, 4, 127-133.

Information on the drugs used in the CR treatment of chronic alcoholism is presented in tabular form replete with generic and trade names, type of drug and action, indications for use, therapeutic rating (effectiveness and toxicity, side effects, contraindications and cautions, recommended dosage and references). Drugs so elucidated include apomorphine, emetine, disulfiram, calcium carbimide, chlordiazepoxide, various phenothiazines, dexamphetamine, ACTH and other corticosteroids and insulin. (15 refs.)

[No address]

2268 Lancet. Adrenaline and schizophrenia. *Lancet*, 1962, No. 7222, 200-201. [Editorial]

Epinephrine (adrenalin) was administered i.v. to 12 chronic schizophrenic men and 13 healthy volunteers (Cardon et al.). The most pronounced variable was a rise in systolic pressure during the 1st 3 minutes which averaged 43% less in schizophrenics. Pulse rate and blood glucose level also rose significantly less rapidly in the latter. Epinephrine was not metabolized more rapidly by schizophrenics, nor did urinary metabolites differ. In another study (Pollin and Goldin) epinephrine was given i.v. to 12 schizophrenic and 12 healthy men. Both groups experienced increased arousal, narrowing of the field of attention, difficulty in communicating and concentrating with feelings of anxiety. Schizophrenics were less able to cope with the experimental situation before the infusion, showing more anxiety towards it than the normal men but less anxiety in response to epinephrine itself. Excretion studies of DL-7-H³-epinephrine-D-bitartrate revealed that none of the infused epinephrine could have been metabolized by adrenochrome or its products in either group. There is yet no indication of confirming the adrenochrome-adrenolutin theory of schizophrenia. (No refs.)

7, Adam Street
Adelphi
London W.C. 2, Great Britain

2269 Tentler, Robert L. Adult neurology. *Illinois Medical Journal*, 1962, 122, 241-242.

Parkinsonism is presently caused by the phenothiazine tranquilizers, which produce typical facies, rigidity, tremor and gait disturbance in addition to dystonia and oculogyric crises. Immediate recovery may be induced with i.v. benztropine (2 mg) or diphenhydramine (50 mg), followed by discontinuation of the phenothiazine. Trigeminal neuralgia responds to heavy doses of diphenylhydantoin. Various neurologic entities and their respective treatments are also discussed. (No refs.)

Stritch School of Medicine
Loyola University Loretto Hospital
Loyola, Ill.

2270 Smith, Jackson A. Adult psychiatry. Newer drugs. Illinois Medical Journal, 1962, 122, 239-240.

The currently available psychoactive drugs include 15 phenothiazine derivatives, 4 Rauwolfia alkaloids, 14 skeletal muscle relaxants and 14 psychic energizers. Potent tranquilizers (phenothiazines and Rauwolfia alkaloids) decrease concern without producing euphoria or increased self-stimuli. The mild tranquilizers (benactyzine and meprobamate) relieve nonspecific anxiety. Drugs of choice among the potent phenothiazines include chlorpromazine and thioridazine. Also, hydroxyphenamate and chlordiazepoxide are the most promising mild tranquilizers. Among antidepressives, amitriptyline, tranlycypromine and imipramine exert minimal side effects. The hydrazine antidepressives, nialamide, isoniazid and phenelzine are contraindicated in patients with a history of liver disease. The most efficacious means of alleviating depression is still ECT. (No refs.)

University of Chicago School of Medicine
Illinois State Psychiatric Institute
Chicago, Ill.

2271 Illinois Medical Journal. No phocomelia in Illinois from Kevadon. Illinois Medical Journal, 1962, 122, 274. [Editorial]

A statewide survey in Illinois compiled from reports submitted by 77 of the 81 doctors who tested thalidomide revealed no cases of phocomelia resulting from thalidomide (Kevadon). All 14 of the pregnant women who received thalidomide during the last month of pregnancy gave birth to normal children. One case of phocomelia was attributed to thalidomide which was purchased in Germany. In the overall testing program very few women of child-bearing age had received thalidomide. (No refs.)

60 N. Michigan Avenue
Chicago 1, Ill.

2272 Potts, Willis J., Frantz, Charles H., Aitken, George T., Kravits, Harvey, Wangerin, Walter M., Filas, Francis L., & Mann, Louis L. The thalidomide tragedy: moral

aspects. Illinois Medical Journal, 1962, 122, 264-268.

With regard to the moral implications of the thalidomide tragedy, 4 physicians and 3 theologians tender their views on abortion and euthanasia. Of the physicians, 1 feels that the present laws should be changed to legalize abortion for such specific cases, 2 others believe that many of these children are of normal or high normal intelligence indicating an excellent possibility of emotional and social habilitation, and the 4th proposes that a therapeutic abortion be performed if the mother gives her consent after having examined her religious beliefs. One theologian would not censure the couple that would decide upon legal abortion if the decision were based upon sufficient medical advice and an earnest examination of their motives. However, another asserts that such abortion and euthanasia are utterly immoral. An eminent Rabbi promulgates the view that failure to prevent such births would be nothing short of a sin against God and man. (No refs.)

[No address]

2273 Lancet. Profession, government, and drug industry. Lancet, 1962, No. 7229, 580-581. [Editorial]

In an address Louis Lasagna gave 8 reasons for the present deplorable condition of the American pharmaceutical industry and offered suggestions for improvement. In the ensuing discussion, other physicians discussed the advent of continuously improved phenothiazine drugs, the reliability of generic name drugs, the fact that doctors kill more people than inferior drugs do and that most American postgraduate medical education is carried out by the pharmaceutical industry. (No refs.)

7, Adam Street
Adelphi
London W.C. 2, Great Britain

2274 Lecks, Harold I., & Kravis, Lillian P. Drug therapy of asthma. Bronchodilators. Clinical Pediatrics, 1962, 1, 125-129.

Tables of bronchodilators used in asthma

therapy include tranquilizing drugs (chlorpromazine, prochlorperazine, promethazine, meprobamate, chlordiazepoxide and hydroxyzine), bronchodilators (epinephrine, ephedrine, ethyllevarterenol, ethylnorepinephrine, etc.), expectorants, oral inhalation therapy, sedatives (phenobarbital and chloral hydrate) and ACTH and corticosteroids. (No refs.)

[No address]

2275 Macdonald, A.D. Habituation and addiction. *Indian Journal of Physiology and Pharmacology*, 1962, 6, 165-173.

A general discussion is given on habituation and addiction in Great Britain in relation to incidence (reportedly much lower than in the United States), prevention, treatment and classification of habit-forming drugs. The responsibility of the pharmacist as well as the medical doctor is emphasized. Brief mention is made of the continued dependency in Great Britain upon morphine rather than synthetic analgesics which have greater preference in the United States. (7 refs.)

Department of Pharmacology
University of Manchester
Manchester, Great Britain

2276 Gilbert, Enid F. An evaluation of some laboratory diagnostic tests in phenylketonuria. *Clinical Proceedings, Children's Hospital of the District of Columbia*, 1962, 18, 328-332.

Laboratory procedures which may be employed in the diagnosis of phenylketonuria include the ferric chloride test, Phenistix test, dinitrophenylhydrazine test, 2-dimensional chromatography and electrophoretic studies. Elevated levels of serum phenylalanine with urinary excretion of abnormal metabolites derived from phenylalanine, tyrosine, ortho-tyrosine and tryptophan constitute a definitive laboratory diagnosis. Many other conditions, particularly hepatic malfunction or insufficiency, can produce positive urinary ferric chloride test findings. Negative urinary findings during the neonatal period should be interpreted with

caution since there is a lag period of several weeks before abnormal metabolites are excreted. Early recognition of phenylketonuria is imperative since treatment with a phenylalanine-deficient diet substantially alleviates symptoms and may possibly prevent symptom development. (15 refs.)

Brackenridge Hospital
Austin, Tex.

2277 Boshes, Louis D. Newer drugs and the nervous system. *Illinois Medical Journal*, 1962, 122, 244-247.

Various drugs used to treat convulsive disorders include diphenylhydantoin, ethosuximide, phenacemide, acetazolamide and chlordiazepoxide. Parkinson's disease responds to trihexyphenidyl, benzotropine, orphenadrine, chlorphenoxamine, parsidol, diphenhydramine, hyoscine and dexamphetamine. Analeptics offer psychomotor stimulation, and antidepressants like imipramine and amitriptyline are also efficacious in alleviating tremor. Severe vascular headaches may be ameliorated with methysergide (UML-491) with appropriate adjuvant therapy. Muscular dystrophy and musculoskeletal disorders may be partially ameliorated with meprobamate and similar compounds. Bemegride, methylphenidate and ethamivan are used to combat drug induced coma. Other drugs are cited which are used in miscellaneous CNS disorders. (No refs.)

Northwestern University Medical School
Michael Reese Hospital and Medical Center
Chicago, Ill.

2278 Feer, H. Schizophrenie und Blutkreislauf. [Schizophrenia and circulation.] *Psychopharmacologia*, 1962, 3, 395-412.

Observations are made on cerebral and general circulation in schizophrenics, psychotic syndromes associated with certain circulatory disorders, somatic sequels of circulatory disturbances, various therapeutic measures, hormones (levarterenol and epinephrine) and drugs affecting circulation. The cardiovascular effects in labora-

tory animals and clinical effects of various psychoactive agents (chlorpromazine, reserpine, chlorprothixene, etc.) is reviewed. The cerebral or general circulatory disturbances of schizophrenics may be secondary to pathological emotional changes; or inadequacies in food and water intake, or catatonic stiffness; they could be associated with somatic constitution or with the etiology of the disease. Present knowledge is uncertain and contradictory. (126 refs.)

Psychiatrische Universitätsklinik Basel
Basel, Switzerland

2279 Greiner, Theodore. Selecting patient participants for drug investigations. *Journal of New Drugs*, 1962, 2, 199-205.

Some of the difficulties which may invalidate inferences from the sample to the population in obtaining patients for drug investigations include definition of the population by accuracy of diagnosis, the broad base clinical trial as opposed to a concentrated focus, utilization of specific clinical entities, bias in the sample, random sampling, personality types in volunteers, patient unreliability, effect of repeated drug trials on a given subject, prevention of man's social nature from upsetting experimental data and the validity of so-called normal subjects who volunteer from a population of prisoners. (11 refs.)

Department of Psychiatry
Veterans Hospital
Houston, Tex.

2280 *Journal of New Drugs*. The new proposed regulations to control new drug testing. *Journal of New Drugs*, 1962, 2, 245-251. [Editorial]

New and more stringent regulations designed to control new drug testing include the following: that the FDA be placed on notice and given full details pertaining to drug distribution for investigational use and that clinical investigations be based on adequate preclinical studies to assure safety and must be properly planned and executed by qualified investigators. Also, the FDA must be kept informed during

the progress of investigations. In notifying the FDA before undertaking clinical investigation with a new drug, manufacturers would be required to provide the following: a summary of all preclinical investigations, copies of all relevant data regarding preclinical information and experience with the drug and names and summaries of training and experience of all personnel who will participate in the investigation. The notice of proposal to amend regulations governing new drugs for investigational use is reprinted in its entirety. (No refs.)

Revere Publishing Company
New York, N.Y.

2281 *Journal of New Drugs*. Generic names of new drugs. *Journal of New Drugs*, 1962, 2, 252-254. [Editorial]

Generic names for psychoactive drugs newly adopted by the AMA-United States Pharmacopeia Nomenclature Committee include propenzolate, diazoxide, piperacetazine and thioridazine. Piperacetazine and thioridazine are both highly efficacious phenothiazine tranquilizers. (No refs.)

Revere Publishing Company
New York, N.Y.

2282 *Journal of New Drugs*. Drug amendments of 1962. Federal Food, Drug, and Cosmetic Act: a summary. *Journal of New Drugs*, 1962, 2, 314-320. [Editorial]

Major alterations in drug provisions of the Federal Food, Drug and Cosmetic Act encompass the following topics: quality manufacturing controls, requirement of proof of effectiveness for new drugs, prohibition of false or misleading labeling of new drugs; suspension or withdrawal of new drug approval on safety grounds, additional grounds for withdrawal of new drug approval, new drug clearance procedure and time limits for federal action, report on experience with new drugs and antibiotics on the market, requirements as to experimental drugs, strengthened factory inspection authority for prescription drugs, registration and periodic inspection of the establishments of drug manufacturers, standardization of nonpro-

prietary drug names, drug names and ingredient formulas on labels and labeling, advertisements for the prescription drugs, batch certification of antibiotics, information to physicians on request, information to the Patent Office from the Department of Health, Education and Welfare, feed additives and effective dates. (No refs.)

Revere Publishing Company
New York, N.Y.

2283 Journal of New Drugs. New Federal regulations for the control of new drug testing in humans. Journal of New Drugs, 1962, 2, 373-376. [Editorial]

New regulations issued by the FDA are designed to strengthen and extend control over new drug investigations. An avalanche of objections from scientists resulted in division of the clinical investigation program into 3 arbitrary sections; phases 1 and 2 relate to clinical pharmacology of the drug, while phase 3 constitutes clinical trials. Reports of all phases must present design modifications in detail. Sponsors must promptly investigate and report any information associated with drug usage which is indicative of significant signs of toxicity. Alarming findings will necessitate discontinuation of clinical testing pending data evaluation. Ordinarily, investigators may withhold the names of volunteers of such information or patients. Extremely important new drugs may be utilized where necessary as lifesaving measures. Enough information must be provided on preclinical data to permit scientific review. Sponsors must discontinue shipments to any investigator who repeatedly or deliberately fails to maintain or proffer his records for inspection. Radioactive drugs for investigational use remain status quo provided they are shipped in accordance with AEC regulations. The full text of the regulations is reprinted for further elucidation. (No refs.)

Revere Publishing Company
New York, N.Y.

2284 Journal of New Drugs. New federal regulations for the control of new drug testing in humans. Journal of New Drugs, 1962, 2, 372. [Editorial]

Reorganization of the Division of New Drugs of the FDA's Bureau of Medicine provides for 5 new branches: the Investigational Drug Branch headed by Dr. Frances O. Kelsey, Controls Evaluation Branch directed by Earl L. Meyers, Medical Evaluation Branch, New Drug Status Branch directed by Dr. John F. Palmer and the New Drug Surveillance Branch. All 5 branches will be under the immediate supervision of Dr. Arthur Ruskin, Deputy Director of the Division of New Drugs, and the general supervision of Dr. Ralph G. Smith, Director of the Division of New Drugs. (No refs.)

Revere Publishing Company
New York, N.Y.

2285 Journal of New Drugs. Generic names of new drugs. Journal of New Drugs, 1962, 2, 122-127. [Editorial]

Generic names of the following psychoactive compounds have been adopted by the AMA-United States Pharmacopeia Nomenclature Committee, in cooperation with the individual manufacturer: phenylramidol, flurothyl, propiomazine, methaqualone and methyl dopa. (No refs.)

Revere Publishing Company
New York, N.Y.

See also 2534

2286 Ziolkow, H.U. Psychodynamische Einflüsse auf den Effekt eines neuen "Psychotonikums" (Phenylpiperidylcarbinol, 1313 Bayer). [Psychodynamic influence on the effect of a new "psychotonic" (phenylpiperidylcarbinol, Bayer 1313).] *Nervenarzt*, 1961, 32, 475-477.

Twenty-eight neurotic female patients (29 years, average age) and 20 healthy female patients (28 years, average age) received a single dose of 10 mg phenylpiperidylcarbinol i.v. The environment conditions (time, place) were the same for all patients. The pulse rate was increased in both groups, more so in the neurotic patients. Blood pressure was also more elevated in this group. The maximal effect was noted after ca. 10 minutes, decreasing after 25 minutes to 3 hours. Side effects consisted among others of dizziness, nausea and headache. Some patients complained of sensations of cold, numbness and heaviness in the extremities. Some in both groups showed impaired ability to concentrate. The euphoria produced was insignificant. In the control group 70% of the patients felt rather well-rested, sometimes gay and generally optimistic. In the neurotic group only 7% showed the same reaction, while dysphoria was present in 82%. Manifestation of neurotic symptoms was found in a 3rd of the patients.

Psychiatrische und Neurologische Klinik
Freie Universität Berlin
Berlin, Germany

2287 Avenarius, R., Fischer, H., & Meyer, J.E. Zur Behandlung der symptomarmen Schizophrenie mit sehr hohen Dosen Reserpin und Orphenadrin. [Treatment of non-florid schizophrenia with very large doses of reserpine and orphenadrine.] *Psychiatria et Neurologia*, 1961, 142, 13-30.

A combination of reserpine (30-90 mg/day) and orphenadrine (300-1200 µg/day), both to control extrapyramidal reactions and as a stimulant, was administered for 3-10 weeks to 29 young male patients with chronic, non-florid schizophrenia characterized mainly by lack of initiative and autism. Maintenance therapy was later given, initially at 6-24 mg/day reserpine

and 200-450 µg/day orphenadrine, reduced finally to 4-12 mg/day reserpine and 200-600 µg/day orphenadrine. Good improvement was obtained in 15 cases, satisfactory improvement in 7 and no improvement in 7. Side effects were difficulty in accommodation, mild tremor, akathisia and restlessness, although 1 case did show a severe Parkinsonian syndrome. Some patients could not be given this combined treatment because of marked intolerance. In 1 older patient, not in the group of 29, treatment with reserpine and orphenadrine may have led to a fatal thrombosis.

Nervenklinik der Universität München
München, Germany

2288 Sherwood, J.N., Stolaroff, M.J., & Harman, W.W. The psychedelic experience. A new concept in psychotherapy. *Journal of Neuropsychiatry*, 1962, 4, 69-80.

LSD (100-200 µg p.o.) and mescaline (200-400 mg p.o.) were administered in a single session to 25 patients (5 with marital problems, 3 alcoholics, 9 with ineffectual personalities, 7 neurotics and 1 with homicidal tendencies) over a 5-month period. Drug ingestion was followed by a tripartite psychedelic experience characterized by the evasive stage, symbolic stage and stage of immediate perception, in which the patient undergoes complete revitalization of self-concept. Overall, 12 were considerably improved, 9 improved and 4 did not improve. The amount of improvement can generally be correlated with the subjects willingness to face himself during the LSD session, and with his acceptance of the abreactive material encountered as indicated by the extent to which he is willing to utilize this material. Optimally, sensitivity and awareness are heightened considerably.

International Foundation for Advanced Study
Menlo Park, Calif.

2289 Webb, H.E., & Lascelles, R.G. Treatment of facial and head pain associated with depression. *Lancet*, 1962, No. 7225, 355-356.

Phenelzine (15 mg t.i.d. or q.i.d.) and imipramine (25-50 mg t.i.d.) were administered to 21 depressed patients with facial and head pain of trigeminal origin (18 with trigeminal neuralgia and 3 postherpetic neuralgia) and 10 with functional facial and head pain. Of those with pain of organic origin, 17 showed a marked response consisting of reestablishment of normal sleep pattern, loss of apathy and listlessness, and considerable pain relief. Of the 10 with psychogenic pain, 8 responded to antidepressants with disappearance of pain. Pain was apparently relieved by treating the underlying depressive state.

Department of Neurology
St. Thomas's Hospital
London, S.E. 1, Great Britain

2290 Feer, H. Beeinflussung schizophrener Zustandsbilder mit Hypertensiva. [Effect of hypertensive medication on schizophrenic conditions.] *Psychopharmacologia*, 1962, 3, 99-104.

Twenty-seven patients (12 men and 15 women, aged 16-60 years) were treated with levarterenol and Hypertensin by i.v. infusion. All patients were schizophrenic (15 catatonic, 8 paranoid, and 4 hebephrenic); 13 patients were in acute stages, 14 were chronically ill (more than 6 months). The rate of infusion was 5-20 μ g levarterenol and 0.5-2 μ g Hypertensin per minute, depending on the blood pressure. The duration of the infusion was 2.5-3 hours. For control, 7 schizophrenic patients received infusions of dioxypheylalanine derivatives. Following the infusions improvement was observed in most patients; those in acute phases reacted more favorably than chronic patients. The infusions with dioxypheylalanine derivatives had no effect. In some patients the behavioral changes were quantitatively evaluated by the IMPA. The morbidity index fell after successful infusion with levarterenol in 41%, with Hypertensin in 43%; in patients who did not respond to the infusions in 13%, and in the controls in 16%.

Psychiatrische Universitätsklinik
Friedmatt
Basel, Switzerland

2291 Lüttke, S., & Koch, R.D. Psychiatrische Schockbehandlung mit Bemegrid. [Psychiatric shock treatment with bemegride.] *Deutsches Gesundheitswesen*, 1962, 17, 1027-1029.

Sixty-one hospitalized patients (25 men and 36 women) with therapy-resistant psychoses (schizophrenia and depressions) were submitted to ECT with bemegride. In order to produce therapeutic convulsions 30-40 cc of 10% bemegride solution were quickly injected i.v., often in combination with suxamethonium (0.4 cc/40 cc). Remissions with subsequent discharge were achieved in most cases after 3-4 treatments. The only side effect noted was occasional postparoxysmal vomiting which could be avoided or controlled with premedication with atropine. In 1 single patient with a therapy-resistant involutional depression, subsequent treatment per os was carried out after discharge (3 cc t.i.d., later on 3 cc b.i.d.). Generalized epileptic equivalents were not clinically observed in this patient. The EEG showed during this phase only a few biphasic spikes. The effect of oral bemegride therapy is considered good.

Nervenklinik der Medizinische Akademie
Magdeburg, Germany

2292 Bram, G. Klinische und Doppelblindversuche mit MH 532 (Gamaquil) bei Spannungskopfschmerz. [Clinical and double-blind studies with MH 532 (Gamaquil) in tension headaches.] *Praxis*, 1962, 51, 648-649.

A double-blind study was carried out in the treatment of tension headaches. Clinical investigation was carried out with phenprobamate [dosage unspecified (Gamaquil)] on 100 patients. Good results were achieved in 80%. The patients were either completely relieved of symptoms or considerably improved. Also placebos and phenprobamate were randomly assigned to 80 patients (5 dropouts) for a period of 2 x 2 weeks (1 tablet t.i.d.). Of the patients who received the drug, 52 were improved (16 considerably, 25 slightly, 11 cured, or, 69%) and 16 were not improved. Of the patients receiving the placebo 7 were im-

proved (9%). Ten percent of the patients reported reduction of tension in addition to relief of pain. No side effects were noted.

Mableton Hospital
Dartford, Kent
Great Britain

2293 Bel, A., Michel, J., & Girard, M. Essai de la thiopropérazine dans le traitement des doubleurs des ulcères gastro-duodénaux. [Trial of thioproperazine in the treatment of pain from gastro-duodenal ulcer.] Archives des Maladies de l'Appareil Digestif, 1962, 51, 941-947.

Thiopropérazine (average dose 3 mg/day p.o.) was administered to 18 patients, the majority over 50 years of age, in combination with trihexyphenidyl, 2.5 mg per day. Three of the patients received 3 mg/day. Duration of treatment was usually 15-45 days. In 15 patients 80% of the pain was relieved immediately and was totally relieved after a maximum of 4-6 days. Patients regained their appetites concomitantly and were able to sleep. Negative results occurred in 3 patients, of whom suffered from actual or suspected ulcerative carcinomas. Ulcers were reduced or cured in 9 radiologically examined patients but this remission may or may not be attributed to the drug. Side effects consisting of parkinsonian symptoms, excitomotor or hypotonic dyskinesias and akathisia were noted in 5 patients who had not received the antiparkinsonian drug concomitantly, but side effects disappeared either after cessation of therapy or after injection of promethazine or other antiparkinsonian drugs.

[No address]

2294 Hankoff, Leon D., Rudorfer, Leon, & Paley, Herbert M. The psychiatric use of pyrbenzindole: a double blind outpatient study. Journal of New Drugs, 1962, 2, 167-172.

Pyrbenzindole (IN 461, 200 mg p.o., t.i.d.) or placebo was administered on a double-blind basis to 50 adult ambulatory patients

with anxiety, average age 38 years, for 2 weeks. Of the 50, 13 failed to complete the course of treatment. Assessment procedures included psychiatric progress reports, the Target Symptom Rating Scale (TSRS), AACL and a global psychiatric rating. The improvement rate for the placebo group was higher (47.6%) than that for the drug group (31.3%), but the difference was not statistically significant. Side effects of both agents were slight, including retardation, nausea, depression, diarrhea, irritability and nervousness. Pyrbenzindole was no more effective than placebo in relieving anxiety and depression and in producing global clinical improvement.

Kings County Hospital Center
Brooklyn, N.Y.

2295 Broussolle, P., & Rosier, Y. Nouvel essai du méprobamate: la forme injectable en thérapeutique hospitalière. [A new trial of meprobamate: the injectable form in hospital therapy.] Annales Médico-Psychologiques, 1962, 120, 1, 130-138.

Meprobamate (400 mg for 3 days, then 800 mg for 20-35 days) was injected into 29 female psychiatric patients, including 7 manic depressives, and 5 cases of senile dementia. Injections were given 1 hour before bedtime. Symptomatic relief of anxiety approximated that obtained with oral administration, while hypnogenic action was considerably greater. Complete disappearance of all abnormal anxiety occurred in 6 cases, great improvement in 11, partial improvement in 7 and failure in 5. Of the 7 depressed psychotics, 5 demonstrated complete or partial improvement. The 5 senile dementia patients showed a new interest in their surroundings. Favorable results appeared 5-6 days after initiation of treatment, duration of the therapy being 3 weeks. Prolongation of treatment beyond this point did not produce new benefits, while suspension of treatment at this point fails even after 2 months to result in any recurrence. However, parenteral treatment should be continued with oral administration of smaller doses. Minor, local side effects consisted of mild pains at the site of injection.

[No address]

2296 Gambs, Pouget, Champeau, Miribel, Marinier, & Auge. Aspects clinique et electroencephalographiques du traitement par le 71-62 R.P. [Clinical and electroencephalographical aspects of treatment with R.P. 71-62.] *Annales Médico-Psychologiques*, 1962, 120, 2, 410-417.

Sixty-three patients were treated for varying periods of time with R.P. 71-62, 50 mg/day p.o., initially increased by 25-50 mg increments until a mean daily dose of 150-200 mg was reached. The drug was injected in 3 cases. Mean duration of treatment was about 1.5 months, with a maximal hospital stay of 8 months. Most patients also received 50 mg/day levomepromazine. Barbiturates (50 mg in the evening) and symptomatic treatment of minor side effects were associated with R.P. 71-62 treatment. Important side effects included generalized epileptic crises and convulsions. Minor symptoms included dry mouth, hesitant speech, faintness on arising, constipation, and some instability. Results were as follows: controlled discharge-16 cases; improvement-27 cases; no effect-17; aggravation-3. EEG disturbances in order of severity were, slowing of appearance of slow delta waves with or without hyperpnea via sensitization and appearance of point waves. The EEG anomalies do not bear any unequivocal relationships to clinical symptoms.

[No address]

2297 Hackstock, H. Alkoholhalluzinose und Delirium tremens und deren Behandlung mit Vitaminen. [Alcohol-hallucinoses and delirium tremens and their treatment with vitamins.] *Therapeutische Umschau*, 1962, 19, 110-113.

Two forms of acute psychoses in chronic alcoholics are discussed: (a) the alcoholic hallucinosis and (b) delirium tremens. Thirteen hospitalized patients were treated; 9 suffered from delirium, 2 had hallucinosis and 2 were chronic alcoholics with severe liver damage. The average age was 55.5 years. The physical findings were comparable in all; all patients had liver damage. The patients were given extensive vitamin therapy. Chlordiazepoxide (75-90 mg p.o.)

was given as supportive therapy. Eight patients were completely relieved of delirium in 2-5 days. One patient died on the 1st day of treatment. The 2 patients with hallucinosis experienced lessening of the intensity of the hallucinations (250 mg thiamine daily).

Kantonale Heilanstalt
St. Pirminsberg in Pfäfers
Pfäffikon, Switzerland

2298 Soulairac, A., & Schaub, Cl. Action du sorbitol sur les atonies intestinales provoquées par les neuroleptiques. [Action of sorbitol on neuroleptic-induced intestinal atonias.] *Annales-Médico-Psychologiques*, 1962, 120, 2, 115-123.

Forty-one patients received sorbitol, 10-30 g/day for 12 weeks. Results were classified as excellent, good and incomplete, on the basis of the number of bowel movements per week: 6-7, 4-5 or 2-3. The distribution of results was as follows: 57% good to excellent, 21.5% incomplete and 21.5% failures. Sorbitol-chlorpromazine antagonism was studied in isolated rat intestine. Addition of 15 $\mu\text{g}/\text{cm}^3$ chlorpromazine to the buffer quickly leads to total atonic immobilization. The presence of sorbitol in the medium before addition of chlorpromazine prevents flattening of the tonus tracing, and when sorbitol is added after chlorpromazine the amplitude of contractions returns to 75-80% of the initial value. Addition of sorbitol alone (20 mg/cm³) leads to an increase in amplitude of contraction and tonus in 2-5 minutes which lasts for 90-120 minutes.

Centre Psychiatrique Ste-Anne
Paris, France

2299 Leichsenring, Frank. Zur Behandlung vegetativer Strahlenreaktionen. [Treatment of functional (vegetative) radiation reaction.] *Therapie der Gegenwart*, 1962, 6, 292-294.

Thirty cancer patients receiving radiotherapy were treated with trifluopromazine for nausea and vomiting. The symptoms were in part due to irradiation of regions

close to the autonomic nerve paths and autonomic ganglia, partially due to "expectation anxiety". Triflupromazine was administered in various dosages: in most severe cases 10 mg i.v., t.i.d.; severe cases 10 mg i.m., b.i.d., and average cases 10 mg p.o., b.i.d. or t.i.d. As maintenance dose 10 mg. t.i.d. was administered orally. The results were as follows: in 18 patients very good to good improvement was achieved, in 10 others the results were satisfactory. No effect was seen in 2 patients. Of these patients, 9 had been treated with phenothiazines and antihistamines [unspecified]. The only side effect seen was fatigue. No pathological findings were observed in blood counts, blood pressure or urine.

Röntgen-und Strahlenabteilung
Allgemeine Krankenhauses Altona
Hamburg-Altona, Germany

2300 Boudin, G., & Lauras, A. L'isocarboxazide (Marplan) dans l'états dépressifs. [Isocarboxazid (Marplan) in states of depression.] *Thérapie*, 1962, 17, 255-272.

Results of isocarboxazid administration (30 mg tablets daily for 2/3rds of the patients) are presented for 90 patients (15 severe depressive syndromes, 43 neurotic depressions, 7 obsessional psychoneuroses, 5 delirium psychoses with depression, 16 organic states, and 4 depressive alcoholics). Duration of treatment varied from 3 weeks to more than 6 months. Side effects include hypotension with or without functional symptoms (but not as severe as with iproniazid) occasional dryness of the mouth, constipation, heightening of the effects of alcohol; occasional dysuria and perspiration; frequent increase in appetite and gain of weight; occasional anxiety. Generally these side effects are moderate in extent and tolerance is superior to that of other thymoleptics. Excellent results were obtained in 16 cases, good results in 30, partial success in 26, doubtful results in 15, and 5 failures. It seems to be especially indicated for melancholia, neurotic depressions, obsessional psychoneuroses and even certain types of organic depressions. The period of latency is 10-20 days after start of treatment. A transient initial hyperexcretion of potassium via the urine was

noted, and some indication exists of damage to liver cells if treatment is continued beyond 6 months. Ambulatory treatment is advisable only when the symptoms, especially anxiety symptoms, indicate no danger of suicide attempts.

Hospital Ste-Antoine
Paris 12, France

2301 Büssow, H. Kombination neuroleptischer Mittel mit vegetativ wirksamen Substanzen. [Association of neuroleptic drugs with substances having autonomic action.] *Medicina Experimentalis*, 1960, 7, 100-111; discussion 112-125.

Patients suffering from melancholia were treated for a 6-8 day period with reserpine [dosage unspecified] or other neuroleptic drugs. After this treatment glutethimide was administered as an additive, at 125-250 mg 3-4 times per day. After a maximal latency period of 2 days, a change occurred, consisting of either increased somnolence or euphoria resembling inebriety, but these effects were transitory, being followed by favorable effects on the melancholic state. In many cases continued treatment with the combination made it possible for the patient to leave the hospital and even to return to work. Extreme cases were also favorably affected by the treatment, stupor being alleviated, and acute hyperkinesia being sedated. Success was also registered in the treatment of acute endogenous psychoses, agitational anxiety depressions, acute paranoid - hallucinatory psychoses, subacute toxic hallucinations, and epileptic emergencies. Paranoid and hallucinatory syndromes persist even after improvement of psyche and drive. The effect of the association is believed to be due to the anticholinergic properties of glutethimide, since the association of other neuroleptic drugs and with anticholinergic drugs has also proved efficacious. The use of a number of antipsychotic phenothiazines is expanded in the discussion.

Allgemeines Krankenhaus
Hamburg-Ochsenzoll
Hamburg-Langenhorn, Germany

2302 Borenstein, P., Dabbah, M., & Blès, G. Etude électroencéphalographique de la thiopropérazine. [Electroencephalographic study of thioproperazine.] *Revue Neurologique*, 1962, 106, 238-243.

In 29 patients, EEG's taken after single 10 mg doses of thioproperazine disclosed the following. Based activity in the form of a regular, well-structured, bilateral, symmetric alpha wave with normal reactivity under hyperpnea but no intermittent light stimulus 12 cases; regular alpha base activity with short theta bursts, 10 cases, 5 of these also showing pointed dysrhythmias; reduced-amplitude irregular alphas, 3 cases; and 3 cases of theta base activity. EEG's taken after a prolonged treatment consisted of: 10 cases of regular alpha base activity; base activity consisting of a regular alpha alternating with or without pointed dysrhythmias, 5 cases; 3 cases of less abundant and less ample irregular alpha base activity; and 1 case of a less ample base alpha overlaid with a large number of rapid rhythms. Cases included hebephrenics, epileptics, hebephrenic-catatonics, delirious psychoses, and other various psychoses. No relationship could be discovered between clinical and EEG results.

Hopital psychiatrique
Veillejuif
Seine, France

2303 Straube, Wolfgang, & Melliwa, Helmut. Zur Dauerbehandlung extrapyramidalen Hyperkinesen mit Perphenazin. [The permanent treatment of extrapyramidal hyperkinesia with perphenazine.] *Nervenarzt*, 1962, 33, 549-553.

Fifty-six hospitalized and ambulatory patients with various forms of chorea, extrapyramidal hyperkinesia, torsion spasm, tic, were treated orally with perphenazine. Adults received at the onset 8 mg t.i.d. or q.i.d.; the dosage was increased and regulated when improvement became evident. Children and young adults were started on 4 mg b.i.d. or t.i.d.; the dosage was increased to 20-24 mg/day. Outpatients received not more than 16 mg per day; others were hospitalized until the dosage

was regulated. The symptoms were favorably influenced and improved in most patients. The only side effects seen were a few isolated cases with stomach discomfort.

Neurologische Klinik der
Städtische Krankenanstalten
Dortmund, Germany

2304 Gayer, W. Beitrag zur Prämedikation bei Kindern. [Contribution to premedication of children.] *Praxis*, 1962, 51, 642-647.

A mixture of chlorprothixene (Taractan) (1-1.2 mg/kg) and hyoscyamine (0.05-0.25 mg depending on weight), injected i.m. 1 hour before surgery was employed in 2439 children during 1961. The advantages were found to be excellent preoperative sedation with rapid onset of anesthesia, potentiation of all anesthetics employed, inhibition of autonomic reflexes, marked reduction of blood loss with only slight decrease in blood pressure, freedom from respiratory depression, simplified induction of anesthesia and postoperative care. Only occasionally were postoperative analgesics required. The only side effect mentioned is occasional skin pallor, which is not considered dangerous. Only 77 complications occurred during this year, and none of these could be attributed to chlorprothixene. The prolonged sedation produced by the drug is not desirable in minor operations on outpatients and in cases where loss of consciousness is feared.

Chirurgisches Abteilung des Kinderspitals
Basel, Switzerland

2305 Bolzani, L. Über die Behandlung von krankheitsbedingten, vorzeitigen Alterserscheinungen mit einem Geriatrikum. [The treatment of early symptoms of aging, due to illness, with a geriatric agent.] *Therapeutische Umschau*, 1962, 19, 24-26.

Two groups of patients were chosen for the treatment with Gerioptil, a combination of novocaine and vitamins [amount unspecified]. One group consisted of 12 patients with the syndrome of reactive

depressions; they did not show any signs of delirium but showed significant organic deterioration. The 2nd group consisted of 9 patients suffering from drug addiction hospitalized for withdrawal. In the latter group, the treatment was started after 3 weeks of complete drug abstinence. The average age of the patients was 48-86. The preparation was administered in the following manner: I) a series of 12 injections of Gerioptil during 4 weeks, with 3 injections weekly; II) a 2nd series for 4 weeks with 6 capsules Gerioptil plus H3 during the 1st week, and 3 capsules during the following 3 weeks; III) a 3rd series of 12 injections as in I). All patients tolerated the medication well; no significant changes in blood pressure and temperature were observed; no pathological changes in blood count and liver function tests were seen. The results were as follows: in group I (11) 1 excellent, 5 good, 1 satisfactory, 2 improved, 2 not improved; in group II (9) 5 good, 2 markedly improved, 1 satisfactory and 1 not improved.

[No address]

2306 Degkwitz, Rudolf. Über die Imipraminwirkung bei Depressionen. [The effect of imipramine in depressions.] *Nervenarzt*, 1962, 33, 450-457.

Six-hundred-and-fifty hospitalized and 150 ambulatory patients were treated with imipramine. The patients were selected on the basis of 3 conditions: 1) only those forms of depression were chosen which did not necessitate sedation; 2) only those patients were selected who had not previously been treated with neuroleptic agents, with MAO inhibitors and ECT, and 3) the treatment had to be continued for a sufficiently long time without interruption. Imipramine treatment alone (75-350 mg) gave 70% good or fair improvement; imipramine in combination with a neuroleptic agent (75-150 mg/day) or ECT gave superior results, and the result of the treatment is seen in 90% of the cases in the 2nd or 3rd week of treatment. Side effects (10% necessitated the interruption of treatment) become evident in the 1st week of treatment (restlessness, increased depression, delirium, lip and tongue spasms).

Results are independent of sex but dependent on age. The chances for improvement in patients over 30 years of age are considerably better. The success of the treatment is independent of the state of depression existing at the onset of treatment. Satisfactory treatment should not be abruptly discontinued.

Universitäts-Nervenklinik
Frankfurt am Main, Germany

2307 Flügel, F., & Itil, T. Klinisch-elektrencephalographische Untersuchungen mit "Verwirrtheit" hervorrufenden Substanzen. [Clinical-EEG investigations on delirium-producing agents.] *Psychopharmacologia*, 1962, 3, 79-98.

Psychotic-delirious conditions were induced with ethotrimeprazine (0.02-0.14 mg per kg i.m. and 0.06-0.25 mg per kg i.v.); phencyclidine (0.02-0.14 mg/kg i.m. and 0.04-0.25 mg/kg i.v.); diethylaminoethylphenobarbital (0.3-1.5 mg/kg i.v.); and phenylisopropyl-oxyacetic-dimethylaminopropylester (0.03 mg/kg i.v. and 10-15 mg orally). One-hundred-and-fifty-six investigations were carried out in 47 patients (26 endogenous depressions, 5 schizophrenics, 7 epileptics, 5 neurasthenics and 4 functional disorders). The following symptoms were observed with increasing dosage: fatigue, difficulty and/or inability to concentrate, disorientation, motor unrest, ataxia, equilibrium disturbances, illusions and hallucinations. The mental disturbances are parallel to disorganization of cortical activity in the EEG, which shows dissolution of alpha rhythm, decrease of voltage and appearance of slow waves and fast activity at the same time. The EEG differentiates these drugs clearly from the "hallucinogenic", and partly from the anticholinergic drugs. The possible therapeutic importance of drug-induced "exogenous" psychoses is pointed out.

Neuro-Psychiatrischen Klinik
Universität Erlangen-Nürnberg
Erlangen, Germany

2308 Grahmann, Hans, & Peters, Uwe H. Durch Psychopharmaka induzierte und pro-

vozierte Psychosen, ihre Psychopathologie und ihre therapeutische Bedeutung. [Psychoses induced and precipitated by psychopharmacological drugs, their psychopathology and therapeutic importance.] *Nervenarzt*, 1962, 33, 398-430.

Psychotic conditions are sometimes precipitated by psychopharmacologic treatment. In 20 patients suffering from different types of compulsive neuroses and from various depressions, psychosis or delirium was intentionally precipitated. Chlorpromazine (100-700 mg i.d.), promethazine (25-300 mg i.d.), chlorprothixene (415 mg i.d.), thioridazine [no dosage given], and orphenadrine [no dosage given] were used, alone or in combination. They were administered initially in large doses which were rapidly increased until delirium was reached. The psychotic state was usually maintained for 2-5 days, up to 10 days. Two patients showed excellent, 9 good and 3 doubtful response: the results were negative in 9. Some of the successfully treated patients had previously not responded to psychopharmacological agents, convulsive drugs and/or psychotherapy. Only cases without organic disorders were treated; massage of the lower extremities and physical exercise was carried out during the psychotic stage. No side effects were experienced. A larger [unidentified] number of patients treated in the same manner did not respond with delirium.

Psychiatrische und Nervenlinik der
Universität Kiel
Kiel, Germany

2309 Fiegel, Georg, & Kukwa, Dietrich. Der regulative Effekt von Hydroxyzin auf die Störungen der Herzrhythmik. [The regulating effect of hydroxyzine on cardiac arrhythmia.] *Therapie der Gegenwart*, 1962, 6, 284-287.

Hydroxyzine pamoate was administered to 67 patients with arrhythmia, caused by functional dysregulation and characterized by extrasystoles and tachycardia; 50 mg t.i.d. p.o. was sufficient for the majority of patients. In severe cases initial doses of 300 mg were given. Two types of response are differentiated: 1) the extra-

systoles were reduced in 24 to 48 hours, and subsequently disappeared completely. The dosage was then reduced to 25 mg t.i.d. Recurrence was rarely seen. 2) The extrasystoles disappeared after brief medication but reoccurred after 4-7 days. Doubling of the initial dosage achieved improvement and, finally, elimination of the extrasystoles. In patients with acute tachycardia best results were achieved with 100 mg i.m., followed by oral medication. The therapeutic effect on functional arrhythmia is good. Concentration and mental alertness are improved rather than dulled. The effect of digitalis is not influenced. No cardiovascular side effects were seen.

Bristol Klinik
Bad Nauheim, Germany

2310 Gottstein, U., Bernsmeier, A., & Steiner, K. Die Wirkung von Nicotinsäure auf Hirndurchblutung und cerebralen Stoffwechsel des Menschen. [The effect of nicotinic acid on cerebral circulation and cerebral metabolism of man.] *Klinische Wochenschrift*, 1962, 40, 772-778.

The effect of nicotinamide and 3-methoxypropyltheophyllin-nicotinate (Complamin) on cerebral circulation and cerebral metabolism was measured in 40 patients suffering from mild and severe arteriosclerosis with the N_2O -method of Kety and Schmidt. Nicotinamide administered by i.v. infusions at a rate of 30 mg/minute, or by single i.v. injection (200 mg), as well as 3-methoxypropyltheophyllin-nicotinate by single i.v. injection (900 mg) had no influence on cerebral circulation and cerebral vascular resistance. The cerebral oxygen- and glucose utilization, and the release of CO_2 , lactic acid and pyruvic acid remained unchanged after the administration of the nicotinic acid preparations.

II. Medizinische
Universitätsklinik München
München, Germany

2311 Hall, John, & Lonie, David. A controlled pilot trial of amitriptyline for treatment of depression in in-patients. *New*

Zealand Medical Journal, 1962, 61, No. 363, 548-550.

On a double-blind basis, amitriptyline (50 mg t.i.d.) was administered to 11 patients with primary depression and placebo to 9 on a random basis; in addition, chlorpromazine (100 mg/day) was given to patients who showed extreme restlessness at night for a period of 4 weeks. Weekly assessment involved 3 criteria: a patient questionnaire, a nursing staff questionnaire and separate interviews with both presiding physicians who rated improvement on a 5-point scale. Within 4 weeks, 4 patients on amitriptyline were markedly improved, whereas only 2 on placebo manifested any improvement. Subjective improvement was also observed in drug-treated patients. Rapid responses were obtained in 6 other patients who were withdrawn from the trial and given ECT, indicating that ECT still remains the treatment of choice in primary depression. The only severe drug-induced effects were hypotension in 1 patient, and dysarthria and ataxia in another. Mild side effects in 3 patients included sweating, dry mouth and blurred vision.

Kingseat Hospital
Papakura, New Zealand

2312 Taverner, D. The hypnotic effects of methaqualone. *Journal of New Drugs*, 1962, 2, 101-103.

Methaqualone (150 or 300 mg p.o.), cyclobarbitol (200 or 400 mg p.o.) or placebo was administered to 24 patients in a general hospital, half of whom were in the acute psychiatric unit, on alternate days in random order. Patients lay quietly in bed and were visited by a nurse every 15 minutes for 4 hours to determine whether or not they were asleep. A maximum number of 16 "sleep reports" could be obtained with each drug dose. Methaqualone (150 mg) resulted in 52 sleep reports out of a possible 384 while cyclobarbitol (200 mg) produced 57 sleep reports. The 300 mg dose of methaqualone produced 111 sleep reports out of 384, and 400 mg of cyclobarbitol yielded 40 sleep reports. This difference was statistically significant, as was the difference between the 2 doses of methaqualone. Methaqualone is a more

effective sleep inducer than cyclobarbitol.

Department of Medicine
The General Infirmary
University of Leeds
Leeds, Great Britain

2313 Fleming, Jack W., & Orlando, Robert. Effect of deanol on attention in the mentally retarded: A reaction time method. *Journal of New Drugs*, 1962, 2, 239-244.

In a double-blind procedure, deanol (75 mg per day p.o.) or placebo was administered to 32 institutionalized retardates, aged 12-25 years, for 55 days after the baseline period, after which the deanol group received 150 mg/day for another 37 days. Attention response to a light stimulus was measured during the last 2 weeks of the initial 3 week baseline period and during the final 2 weeks of the study. A distracting stimulus (orange light, buzzer or combination thereof) was presented simultaneously with a green light stimulus once during each block of 10 trials. Deanol effect was estimated by comparison of reaction time performance before and after drug administration, as well as between drug and placebo groups. Statistical analysis of mean reciprocal reaction times for all trials, distracting trials and trials following distraction revealed no evidence that deanol greatly improved attention, as reflected in overall reaction time. Some positive drug effect is indicated, however, by resistance to attention loss, as well as increased alertness or sensitivity to sudden, novel stimuli.

Rainier School
Buckley, Wash.

2314 Terry, James G., & Teixeira, Theodore C. Nalorphine testing for illegal narcotic use in California: Methods and limitations. *Journal of New Drugs*, 1962, 2, 206-210.

Nalorphine (3 mg) is injected s.c. in suspected narcotic users, before and after which pupillary size is measured by a pupillometer to the nearest 10th of a millimeter. During a standard clinic session,

if the 2nd pupillary diameter exceeds the 1st by 0.25 millimeter or more, the test is considered positive and the patient is thoroughly examined for needle marks and other signs and symptoms of narcotic use. Patients are permitted to leave the clinic if the pupil remains the same size or constricts. In California, parolees receive 5 tests per month while probationers receive 2. Physical similarities are observed in clinic design. Nalorphine clinics are located throughout the state of California. One of the detriments of the nalorphine test is that too much emphasis is placed on pupillary measurement with no additional evidence of narcotic use. The test should be considered only as a diagnostic aid. Correlation of the pupillary test in 419 subjects with chemical tests of urine revealed that pupillary tests agreed with the chemical tests in 85% of the cases, 339 having been negative and 18 positive by both procedures. The chemical tests were more sensitive in 28 instances. Nalorphine induced side effects which occur in 5-10% of those tested include dizziness, light-headedness, tiredness, peripheral vascular effects, ataxia and euphoria. Nalorphine testing is effective as a restrictive procedure.

Santa Rita Rehabilitation Center
Pleasanton, Calif.

2315 McCusker, Kenneth, Ota, Kay Y., Michaux, William W., & Kurland, Albert A. N-(2,5-dimethyl-1-pyrrolyl)isonicotinamide in the treatment of the inactive chronically psychotic patient. *Journal of New Drugs*, 1962, 2, 232-238.

In the 1st portion of a 2-part study, 39 men (31 schizophrenics, 6 mental defectives with psychosis and 2 CBS), aged 27-64 years, average duration of hospitalization 19.0 years, received placebo or N-(2,5-dimethyl-1-pyrrolyl)isonicotinamide (SQ-3242) (50 mg q.i.d. for 2 weeks, 100 mg t.i.d. for 2 weeks and 100 mg q.i.d. for 1 week) on a randomly assigned double-blind basis for 5 weeks, followed by a 2 week medication free observation period. Routine laboratory analyses were performed before and after treatment. Patients were evaluated on a double-blind basis by

means of the MACC Behavioral Adjustment Scale, the Psychotic Reaction Profile (PRP) and weekly clinical interview assessments by 3 psychiatrists. The 2nd phase of the study involved administration of SQ 3242 (100 mg q.i.d. for 1 week, 100 mg t.i.d. for 2 weeks with 200 mg at bedtime, 200 mg t.i.d. with 100 mg at bedtime for 1 week and 200 mg q.i.d. for 1 week) for 6 weeks to 9 men (7 chronic undifferentiated schizophrenics and 2 mental defectives with psychosis, average age 47.3 years, who were members of the placebo group in the 1st phase of the study. One psychiatrist evaluated patient response. Analysis of covariance for MACC and PRP scores yielded no significant differences. No decisive therapeutic effect was observed from the drug in the 1st or 2nd phase. Moderate slurring of speech and other basal ganglion symptomatology occurred in 3 patients with medium to high drug dosage. Seven drop-outs were observed in toto.

Research Department
Spring Grove State Hospital
Baltimore 28, Md.

2316 Kurland, Albert A., McCusker, Kenneth, & Michaux, William W. Clinical trial of haloanisone with hospitalized psychiatric patients. *Journal of New Drugs*, 1962, 2, 352-360.

Haloanisone (15-150 mg/day p.o.) was administered to 30 patients (2 acute undifferentiated schizophrenics, 9 paranoid schizophrenics, 2 schizoaffective schizophrenics, 1 manic-depressive, 2 depressive reactions, 1 alcoholic, 1 adolescent adjustment reaction, 1 acute brain syndrome and 1 CBS) for 5 weeks. Patients were evaluated by 2 psychiatrists at weekly intervals. Results revealed that 3 (10%) were markedly improved, 2 (7%) moderately improved, 12 (40%) minimally improved, 9 (30%) essentially unchanged and 4 (13%) worse. Side effects occurring in 20 patients were primarily extrapyramidal in nature and generally reversible with appropriate medication. Severity of side effects precluded further treatment in 5. Physical and laboratory observations yielded no evidence of serious toxic effects. Statistical analysis revealed significant differences in sex and

duration of treatment. Haloanisone was most efficacious in the agitated, hallucinated, hyperactive patient.

Department of Mental Hygiene
State of Maryland
Baltimore 1, Md.

2317 Krakowski, Adam J. Treatment of depression with imipramine (Tofranil) and imipramine combined with promazine. *Journal of New Drugs*, 1962, 2, 56-62.

In a double-blind study, 216 depressed patients, aged 19-81 years, including neurotic, involutional and psychotic depressives, were treated with imipramine, promazine, or with small amounts of other tranquilizing agents. Complete recovery or marked improvement occurred in 77% of 178 patients treated with imipramine alone. The daily dosage was 75-100 mg with increases in most of the cases to 150 mg/day. Anxiety or agitation resulted in tranquilizer administration: phenothiazines in 57%, meprobamate in 10% and other tranquilizers in 23% [sic]. The treatment period was usually 2-3 months. Complete recovery was observed in 57% of the patients with severe depression and 43% of the cases with milder depression. The most frequent side effects were dry mouth in 33%, sweating 33%, headache 12%, constipation 11%, anxiety 9% and agitation in 8%. Fatigue, drowsiness, extrapyramidal reactions, postural hypotension and other untoward effects were also noted. In the 38 patients who were treated with imipramine and promazine, there was a recovery rate of 82%. Imipramine and promazine were begun at a ratio of 1:1 (100 mg/day each) then increased or decreased as found necessary. With imipramine alone, an excellent response was obtained in every case of manic depression. When imipramine plus promazine was used, good results were obtained in the depressions commonly associated with marked anxiety, with agitation, and even with insomnia. The side effects were similar to those with imipramine alone, with the most frequent complaints being dry mouth and sweating.

[No address]

2318 Sörgel, H.-J. Klinische Erfahrungen mit dem Psychotonikum Centedrin. [Clinical investigation with the psychotonic "Centedrine".] *Deutsches Gesundheitswesen*, 1962, 7, 256-259.

Twenty-eight hospitalized and ambulatory patients were treated with Centedrine [sic: methylum piperidyl-phenylacetum hydrochloricum; related to piperylone]. Twelve of these patients were suffering from endogenous depressions, 4 displayed depressive-paranoid symptoms due to cerebral arteriosclerosis, 5 had involutional depressions, 4 had developed organic complaints due to neuroses of long standing; 2 suffered from functional dysregulation, and 1 was in a narcolepsy-like condition. The treatment was initiated with 1-2 tablets b.i.d., and was increased to 1-2 tablets t.i.d. The duration of treatment was 2-8 weeks for hospitalized patients, and up to 3 months for ambulatory patients. The effect was very good in 12 patients, good in 11, fair in 4 and insignificant in 1. Frequent laboratory investigations of blood and urine revealed no pathology. Withdrawal of the medication had no negative effects.

Nervenklinik der Medizinische Akademie
Erfurt, Germany

2319 Lereboullet, J., Benoit, Ph., & Ledoux, M. Action anxiolytique du chlordiazépoxide. [Anxiolytic action of chlordiazepoxide.] *Thérapie*, 1962, 17, 1005-1009.

Thirty-five mixed cases including some cases of cranial trauma were treated with oral doses of chlordiazepoxide (30-100 mg per day). Rarely the drug was used i.m. The common dosage was 30-40 mg/day and maintenance 20-40 mg/day. In some cases chlordiazepoxide was associated with other antidepressants or neuroleptics. Where anxiety was the chief component, 11 cases, excellent results were obtained in 5 and definite improvement in 6. The drug suppressed the anxiety of depression but not depression per se. Reactions with psychotic states were poor. Tolerance was excellent. One case of digestive disorder, and 1 case of erythematous eruption occurred.

Hospice de Bicêtre, Kremlin-Bicêtre
Seine, France

Clinical studies
Abstracts 2320-2324

2320 Madalena, J.C. O emprêgo do clorprotixeno (RO 4-0403) na psicose maníaco-depressiva. [The use of chlorprothixene (RO4-0403) in manic-depressive psychosis.] O Hospital, 1962, 61, 199-200.

Success was obtained in 4 cases of manic excitation with suppression of crises within 48 hours through the i.m. use of 30 mg chlorprothixene in the morning and afternoon.

Psiquiatria do Hospital da Ordem Terceira de S. Francisco da Penitência
Universidade do Brasil
Rio de Janeiro, Brazil

2321 Dos Santos, Oswaldo. Resultados clínicos do uso da trifluopromazina em esquizofrênicos com mais de dois anos de doença e submetidos a vários tratamentos. [Clinical results on trifluopromazine in schizophrenics ill for more than 2 years and submitted to various treatments.] Revista Brasileira de Medicina, 1962, 19, 574-578.

Five schizophrenic hospitalized women, including 3 paranoid reaction were treated with trifluopromazine, initially 10 mg i.m., then 50 mg tablets, both t.i.d. Doses were raised until maximum daily dosage reached 300-600 mg for 10-23 days. The onset of extrapyramidal reactions in these patients was correlated with improved mentation in all cases. Insomnia, anxiety, iron deficiency anemia, amenorrhea, galactorrhea and vomiting were noted as side effects as well as slight hypotension in 1 case. Complementary treatment consisted of barbiturate, B-complex vitamins, iron sulphate and an antispasmodic. Total remissions were obtained in 3 patients and partial remissions in 2. These results were superior to those obtained previously in these patients using fluphenazine or chlorpromazine.

[No address]

2322 Nagle, Gilberto J. Tratamento da úlcera péptica gastro-duodenal pela associação do brometo de clidinium à Clordiazepoxida. [The treatment of gastro-duodenal peptic ulcer with the combination

of clydinium bromide and chlordiazepoxide.] O Hospital, 1962, 61, 89-92.

Ten peptic ulcer patients, affected with various grades of emotional tension, were treated with 1 Librax tablet t.i.d. (5 mg chlordiazepoxide and 2.5 mg clydinium), with supplemental aluminum hydroxide. Optimal results were obtained in 20 days with 7 patients—disappearance of epigastritis and emotional tension.

Faculdade Nacional de Medicina
Rio de Janeiro, Brazil

2323 Eilenberg, D. Nialamide in the intravenous treatment of depression. Staff Meetings of the Mayo Clinic, 1962, 37, 367-371.

Nialamide did not show therapeutic efficacy when given i.v. to 21 patients with severe depression. Each patient received 500 mg nialamide i.v. in 1 liter of glucose saline each day for 6 consecutive days; each administration lasted 3 hours and was followed by a rest period of 2 hours. A 14 item rating scale for depressives modified from Hamilton was used in evaluation along with laboratory tests used to monitor side effects. The depressive ratings of 17 out of 21 patients decreased after nialamide treatment, and this decrease was often due to lessening of anxiety, agitation and insomnia. Continuation of depressive moods was of sufficient intensity to warrant prescription of ECT in 15 out of the 21. Also nialamide was continued p.o. in doses of 100 mg t.i.d. for patients recovering sufficiently to warrant discharge. Treatments were remarkably free of side effects; 4 patients had some hypotension and 3 had headache and/or nausea.

Mayo Clinic
Rochester, Minn.

2324 Kammerer, Th., Singer, L., Geissmann, P., Depoutot, J.-C., & Gutbug, Th. Résultats thérapeutiques du 2028 M.D. [Therapeutic results with MD 2028.] Annales Médico-Psychologiques, 1962, 120, 1, 402.

Sixty-three agitated patients benefited from

treatment with MD 2028 [dosage unspecified]. The drug was particularly active in suppressing psychomotor paroxysms. It potentiates effects of phenothiazine derivatives. The side effects were extrapyramidal reactions, cardiovascular and respiratory disturbances which necessitate strict medical surveillance. The drug is contraindicated for combination with phenothiazine derivatives.

[No address]

2325 Sampaio, Benedicto Arthur, Amaro, Jorge Wohwey Ferreira, & Meyer, Luiz. Do emprêgo do "clordiazepóxido" no delirium tremens e na alucinose alcohólica. [On the use of chlordiazepoxide in delirium tremens and alcoholic hallucinosis.] O Hospital, 1962, 62, 131-155.

Twenty-three cases of delirium tremens with florid symptomology and 2 cases of alcoholic hallucinosis were treated with chlordiazepoxide: 20 mg 4 or 6 times a day p.o., 50 mg q.i.d. or 8 times a day and 100 mg q.i.d. 8 times a day. Further, 100 mg chlordiazepoxide was given i.v., q.i.d. in 2 cases followed by 50 mg q.i.d., p.o. Of 18 cases treated orally, 50% recovered in 2 days and 30% in 3 days, compared to results with routine methods which were 40% recovery in 3 days, and 30% in 2 days. One hallucinatory case recovered in 6 hours, the other in 48. Tremors were reduced in 60% of the cases in 24 hours. Ataxia due to treatment was noted in 2 patients and disappeared on cessation of the drug.

Departamento de Assistência e Psicopatas
do E. de São Paulo
São Paulo, Brazil

2326 Tabbal, Gabriel. Algumas observações com o uso do "Librax". [Some observations on the use of Librax.] O Hospital, 1962, 62, 845-846.

Seven cases of spastic colitis, 4 of biliary spasm and 4 of duodenal ulcer were treated with Librax (clidinium combined with chlordiazepoxide) (2.5 mg plus 5 mg respectively per tablet). Three tablets were given daily.

In the 1st condition results were 6 excellent and 1 good, in the 2nd 3 excellent and 1 good, and in ulcer patients 3 excellent and 1 good. Also, 3 cases of tension headache were treated with alleviation and diminution of crises.

Soc. Gastreenterol.
Rio Grande do Sul
Brazil

2327 Medrado, Valdir C., & Conde, Daisy. Avaliação clínica e experimental de um novo analéptico: 3-metil-7-metoxi-8-dimetilaminometil-flavona. [Clinical and experimental evaluation of a new analeptic: 3-methyl-7-methoxy-8-dimethylaminomethyl-flavone. O Hospital, 1962, 62, 1077-1090.

3-Methyl-7-methoxy-8-dimethylaminomethyl-flavone was studied for acute toxicity (i.p. in rats), convulsant activity, analeptic activity in rats in comparison with other respiratory stimulants, and action on respiration, blood pressure, heart rate, ECG and EEG, the latter in dogs. In rats the LD₅₀ is 5.3 mg/kg while the CD₅₀ is 4.9 mg/kg. Pentobarbital treated rats were used in tests of analeptic activity: when compared to nikethamide, pentetrazol and Micoren, the analeptic activity of 3-methyl-7-methoxy-8-dimethylaminomethyl-flavone was greater. There were no changes in blood pressure and heart rate after i.v. administration in dogs, while the depth of breathing was markedly increased. Further there were no significant effects in the EEG. One hundred patients scheduled for dilatation and curettage were selected for clinical evaluation and 50 of these were anesthetized with pentobarbital (8-10 mg/kg). The 2nd group of 50 was given a preliminary dose of 0.16 mg/kg of a new analeptic before pentobarbital administration, and a 2nd dose was applied near the end of the operation. Results were encouraging, i.e., marked increase in pulmonary ventilation. The drug showed advantages in relation to the resuscitation of asphyxiated newborns, and newborns depressed by anesthetic and analgesic drugs.

Universidade da Bahia
Bahia, Brazil

Clinical studies
Abstracts 2328-2332

2328 Dos Anjos, Edgar Soares. O clorprotixeno em psiquiatria de ambulatório. [Chlorprothixene in the psychiatry of ambulatory patients.] O Hospital, 1962, 62, 739-745.

Of 12 patients treated with chlorprothixene, 3 were paranoid schizophrenics while the others were suffering from various types of neuroses. The drug was given in the form of 15 mg tablets, 15-45 mg per day, sometimes combined with psychotherapy. Results with the 3 schizophrenics were considered excellent in relation to the suppression of hallucination and improved behavior. With 6 cases of anxiety results were: 3 excellent, 2 good and 1 poor, while with the 3 remaining cases, obsessive-compulsive reaction, results were 1 excellent and 2 good. That is, improvement occurred in 11 out of the 12 cases. Side effects were practically absent (drowsiness in some patients at the beginning of treatment).

Psiquiatra do I.A.P.I.
Rio de Janeiro, Brazil

2329 Pünder, Norma de Araújo. Contribuição ao estudo da síndrome pré-menstrual. [Contribution to the study of the premenstrual syndrome.] O Hospital, 1962, 62, 857-864.

The combination 1 mg fluphenazine, 2.5 mg benzhydroflumethazide and 500 mg KCl was administered to 15 patients with premenstrual syndrome, aged 18-41 years. Nine had previously been unresponsive to hormonal or antispasmodic therapy. Seven cases received the combination for 4 successive months and the 8 others received it alternating 1 month on drug and the other on placebo for the 4 months. Treatment was always initiated 10 days preceding expected menstruation. After 4 months, 4 were in complete remission, and 3 had markedly improved. No toxicity was recorded.

[No address]

2330 Marques, Jamerson Rodrigues, Lino, Renato, Freitas, Abelardo, & Luiz, Augusto

Cesar. Emprêgo da triflupromazina no pós-operatório. [The postoperative use of triflupromazine.] O Hospital, 1962, 62, 789-794.

Triflupromazine has a definite advantage over opiates in postoperative analgesia. Triflupromazine has been used as the only postoperative medication in 365 cases and only 5 cases of side effects were reported: 2 nasal congestion and 3 insomnia, both disappearing rapidly after cessation of the drug. Immediately after surgery 10 mg was given continued t.i.d. then b.i.d. for a total of 3 days or more.

Santa Casa de Misericórdia
Belo Horizonte, Brazil

2331 Da Silva, Antonio Ribeiro, Barros J. James Castro, Meirelles, Paulo, & Oliveira, José Domingues. Flufenazina na esquizofrenia. [Fluphenazine in schizophrenia.] Revista Brasileira de Medicina, 1962, 19, 528-531.

Twenty-four hospitalized schizophrenics, 21 women and 3 men, were treated with 2.5-20 mg (initial average 6.5 mg) fluphenazine daily. This dose was increased by 2.5 mg per day to reach a maximum daily dose of usually 15 mg/day, however 1 case received 60 mg/day. The drug was usually given every 8 hours p.o., but in psychomotor crises it was used i.m. The average length of treatment was 45.66 days. In decreasing order of frequency, side effects were muscular hypertonia and drooling, alteration in pulse and blood pressure, changes in walking and dermatologic reactions, fixed facies, tremor most attributable to extrapyramidal reaction. By the 8th day 70% of the patients were showing extrapyramidal symptoms. Sixteen remissions were obtained and 4 definite improvements, contrasted to 3 failures. Also, death occurred unrelated to treatment.

Instituto Raul Soares
Belo Horizonte, Brazil

2332 Ban, T.A., & Lehmann, H.E. Clinical trial with desmethylinipramine (G-3502). A new antidepressive compound. Canadian

Medical Association Journal, 1962, 86, 130-1031.

Demethylimipramine (75-225 mg/day p.o.) was administered to 25 depressive patients (3 manic-depressive, 7 involuntional melanolia, 4 schizophrenic or schizoaffective and 1 neurotic depressive reaction), average age 47 years, for 10 weeks. Two psychiatrists provided independent evaluations utilizing the Lehmann, Cahn and deVerteuil rating scale to evaluate the intensity of depressive symptoms. Patients were rated daily during the 1st week, 3 times the 2nd, twice the 3rd, and weekly thereafter. Response was excellent in 13, good in 5, fair in 3 and nonexistent in 4. Side effects included insomnia in 4, hypomanic states in 2, and 1 case each of drymouth, sweating and mydriasis. Definite extrapyramidal symptoms were exhibited by 1 patient. Medication was discontinued in 2 due to severity of side effects. Demethylimipramine appears to exert less troublesome side effects than imipramine, and its efficacy exceeds that of the mother compound.

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Canada

2333 Taylor, Alfred M. Acute intermittent porphyria—relief of severe pain after treatment with chlorpromazine hydrochloride. Report of a case. Cleveland Clinic Quarterly, 1962, 29, 204-209.

A 26-year-old woman with severe pain secondary to acute intermittent porphyria received phenobarbital (1.5 grains at bedtime for 8 doses), prochlorperazine (10 mg i.v.), EDTA, BAL, diphenylhydantoin, penicillin [dosages unspecified], chlorpromazine (25 q.i.d.—50 mg 6 times daily p.o.), ACTH, meperidine, etc. for various periods of time in an attempt to alleviate abdominal pain. Prompt and complete pain relief followed administration of 50 mg chlorpromazine. Gradual improvement was observed in apnea and bulbar speech, with diminution of orthostatic hypotension despite persistent sinus tachycardia. Maintenance medication comprised chlorpromazine, 50 mg q.i.d. Physical examination the

following year revealed no evidence of autonomic imbalance, improvement in peripheral neuropathy and amelioration of other symptoms.

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Philadelphia, Pa.

2334 Vestre, Norris D., Hall, Wilson B., & Schield, Burtrum. A comparison of fluphenazine, triflupromazine, and phenobarbital in the treatment of chronic schizophrenic patients: a double-blind controlled study. Journal of Clinical and Experimental Psychopathology & Quarterly Review of Psychiatry and Neurology, 1962, 23, 149-159.

Ninety-three hospitalized schizophrenics were randomly assigned to triflupromazine, fluphenazine and phenobarbital on a double-blind basis for 12 weeks. Average daily dosage reached by the end of the period was: 130 mg triflupromazine, 10 mg fluphenazine and 130 mg phenobarbital. The PRP and MMPI were used before, after 4 and 12 weeks of treatment. The 2 phenothiazines were more effective than phenobarbital; 5 patients dropped from the study were in the phenobarbital group. On the basis of the PRP, triflupromazine was superior to phenobarbital, while fluphenazine was not. No difference in the overall effectiveness of the 2 phenothiazines was found. The difference between fluphenazine and phenobarbital was detected in "thinking disorganization", where triflupromazine was superior to phenobarbital. Also, the side effects were very infrequent, i.e., parkinsonism.

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2335 Burner, M., Bieri, J., & Calanca, A. Bilan préliminaire de l'essai du traitement des dystonies neuro-végétatives par un médicament organo-magnésien, le Cirtonal-N. [Preliminary evaluation of therapy of autonomic dystonias with an organic magnesium drug, Cirtonal-N.] Praxis, 1962, 7, 187-190.

Forty-five patients, suffering from autonomic dystonias, including alcoholics, neurotics and schizophrenics, were treated either with organic magnesium, Cirtonal-N, i.v. (34 patients), or with placebos (11 cases). Of those receiving the drug, definite improvement was noted in 6, good results obtained in 21, doubtful effects in 3, and no effect in 4. Only 5 of the 11 patients receiving placebos reported good results, the remaining being either doubtful or zero. Injections were well tolerated.

Policlinique Psychiatrique
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Lausanne, Switzerland

2336 Lanter, R., Weil, J., & Roth, M. Note à propos de l'utilisation diagnostique et thérapeutique des drogues hallucinogènes (mescaline-L.S.D. 25). [Note on the diagnostic and therapeutic use of hallucinogens (mescaline-LSD 25).] *Annales Médico-Psychologiques*, 1962, 120, 2, 244-252.

Fourteen patients, institutionalized sex perverts and recalcitrant chronic alcoholics, were placed under hallucinogenic therapy. All of these subjects shared certain personality traits, namely, impulsiveness, avidity, and "orality". Patients received either mescaline (600-1400 mg) orally or by injection, or LSD (100-800 mg) or an association of the latter with apomorphine, this combination being administered to alcoholics. Generally the hallucinogens can constitute an important adjunct to other therapeutic methods. The reaction to mescaline seems to be more marked than to LSD. Typical reactions are stupor with inhibition and mutism, or agitation. Subjects report greater suggestibility, analogous to that of hysterical states. Their diagnostic value so far has resided in their reinforcement of latent psychotic or neurotic symptoms.

[No address]

2337 Delachaux, A., & Schwed, S. A propos de l'utilisation du Tofranil dans un service de gériatrie de réhabilitation fonctionnelle. [On the use of Tofranil in a geriatric rehabilitation clinic.] *Praxis*, 1962, 23,

597-600.

Imipramine (Tofranil) and placebos were used in the treatment of 40 patients, aged 50-90 years. Dosage was 75-200 mg/day, usually 150 mg/day. Both placebo and drug were administered alternately for 3 week periods. Most of the patients (31) suffered from arteriosclerosis; there were 7 cases of hypochondriasis, 3 mental confusion etc. Effects of drug and placebo on the same patient were compared, with the following results: neither drug nor placebo had any effect-8 cases; imipramine action fair or variable, but better than that of the placebo-12 cases; imipramine action good, placebo action negative-13 cases both drug and placebo effective-7 cases. Side effects were difficult to determine in view of the multiplicity of basic troubles. Dry mouth was noted in 5 patients, sweating in 3 patients, 1 grand mal crisis, somnolence in 2 cases and confusion in 4. Recommended dose is 60 mg/day, caution being necessary in older persons.

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2338 Knick, B. Psychische und Organotropen Wirkungen eines neuen Imipraminderivates (Amitriptyline) bei internistischen Indikationen. [Psychic and organotropic effects of a new imipramine derivative (amitriptyline) in the treatment of internal conditions. *Therapie der Gegenwart*, 1962, 101, 11-16.

Amitriptyline was administered orally to 149 hospitalized patients for 3 weeks to 5 months, doses being increased gradually from 25-75 mg at the start, to a maximal dose of 375 mg per day. The antidepressive effect of the drug depends upon the initial doses, 150 mg per day having proven the most effective. Older patients are more sensitive to the drug than younger ones. Frequency and intensity of side effects are very low, consisting chiefly of tachycardia (4.6% of the patients), disturbances of accommodation (4.2%), hypersecretion (4.1%), and dry mouth (3.8%). Other symptoms include nausea, vomiting, dizziness, extrapyramidal symptoms and

parasthesia. It was concluded by the experimenter that amitriptyline had an excellent effect on depression. Maintenance doses of 25 mg per day are recommended for the patient.

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Mainz, Germany

2339 Faidherve, J., Ouachi, S., Dongier, M., & Gastaut, H. Etude comparée de l'action de deux anti-épileptiques nouveaux, le N 3 et le N 5. (Note préliminaire à propos de 100 observations). [Comparative study of the action of 2 new antiepileptic drugs, N 3 and N 5. (Preliminary note on 100 observations).] Annales Médico-Psychologiques, 1962, 120, 1, 746-751.

Two hydantoin derivatives, N 3 and N 5, were administered to 50 epileptic children, 1-18 years old and 50 epileptics, 18-60 years old. Children were hospitalized, while adults were ambulatory, with much less severe disorders. Daily dosages varied, according to the condition of the patient, from 3-10 tablets/day. Duration of treatment was highly variable, lasting as long as 26 months. Leukopenias and modifications of the leukocytic family consisting of neutropenia and compensatory lymphocytosis occurred in about half the cases. Occasional rashes were observed in the children but never in adults. Neither N 3 or N 5 had any effect on the crises of 2 patients; in 19 cases these were intensified in terms of either frequency or severity, and in 18 a clearcut diminution of number and/or severity of convulsions was noted with complete disappearance of convulsions in 11. Possibility of improvement seems to be linked to the type of EEG tracing, since 54 of the 71 patients with indifferent or poor results displayed diffuse discharges, while 21 of the 29 cases in whom improvement was noted showed a very limited focus. None of the patients with bisynchronous multipoint waves showed any improvement. The drugs are most useful in partial epilepsies, particularly those with concomitant behavioral troubles.

No address]

2340 Borenstein, P., Dabbah, M., Blès, G., Roussel, A., & Rosemberger. Etude clinique et électroencéphalographique de l'éthybenzatropine (1) (U.K. 738 ou tropéthdryline) utilisée en administration exclusive. [Clinical and EEG study of ethybenzatropine (U.K. 738 or tropethdryline) used by itself.] Annales Médico-Psychologiques, 1962, 120, 1, 288-295.

Thirty-eight male patients (10 schizophrenics, 10 epileptics with behavioral and character disorders and 18 miscellaneous psychotics) were treated with methylbenzatropine [sic: ethybenzatropine (20 mg/day, i.m., i.v. or i.p.)] for a total of 1079 days, mean duration of therapy varying from 11-20 days in 14 cases, and 20-40 days in 19 cases. In 16 patients, side effects included mydriasis, visual fatigue, dry mouth, asthenia, daytime somnolence, urine retention and autonomic disturbances. Neurological sequelae were rare and mild. No psychic effects were noted in 22 cases, some improvement in 10, and aggravation in 8. After drug administration no EEG modification was noted in 27, clearcut amelioration of alpha-base activity in 14, and accentuation or exacerbation or previously existing anomalies in 9. EEG tracings after a prolonged period of treatment were generally the same as those obtained after a single dose. The drug is not epileptogenic, but remains "active" in almost half of the convulsive disorders.

Centre de Médecine Psycho-Somatique
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Villejuif, France

2341 Goldstein, Leonide, Murphree, Henry B., Sugerman, A. Arthur, Pfeiffer, Carl C., & Jenney, Elizabeth H. Quantitative electroencephalographic analysis of naturally occurring (schizophrenic) and drug-induced psychotic states in human males. Clinical Pharmacology and Therapeutics, 1962, 4, 10-21.

Drohocki's integrator was used in this study made up of 3 parts: the characteristics of the quantified EEG of normal subjects without drug and after placebo; measurements obtained from EEG's of male chronic schizophrenics, and effects

on EEG's of LSD administered to normal subjects and schizophrenics. Analysis of the quantified EEG of the left occipital lead of 21 normal male subjects revealed an average coefficient of variation in electrical energy of 15.4%. In 25 male chronic schizophrenic patients, the mean coefficient of variation was 8%. Placebo administration did not produce any significant change in either group. In the normal men, oral dosage with 0.3 μ g/kg LSD produced a 33% decrease in variability without significant change in the mean energy content of the EEG. When the LSD dose was increased to 1 μ g/kg, a 25% decrease in variability and 23% reduction of the energy content of the EEG followed. In schizophrenic patients, LSD at 1 μ g/kg orally did not affect the mean energy content but produced a 47% increase in variability. The EEG of male institutionalized chronic schizophrenics tends to be hyperregulated. Similar hyperregulation is produced in normal volunteers by threshold and larger doses of LSD.

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2342 Kameda, Hideaki, Hidaka, Yasuhiko, & Furukawa, Tadayuki. Changes in electroencephalogram following administration of chlordiazepoxide. *Folia Psychiatrica et Neurologica*, 1962, 16, 15-22.

EEG changes following administration of chlordiazepoxide (20-40 mg/day) were studied in 13 patients (9 epileptics, 2 epileptoid character disorders and 1 each head trauma and encephalomalacia), aged 6-20 years, for 1 week to 57 days. Marked improvement was shown by 6 patients, moderate improvement by 5 and no change or no evaluation in 2. A decrease of high-voltage paroxysmal dysrhythmia was associated with clinical improvement. Paroxysmal activity provoked by activating procedures like photic stimulation, hyperventilation and i.v. injection of bemegride was considerably reduced following drug administration. Fast waves, about 20 per second, increased predominantly in the frontal and central regions in most cases. This suggested a

similarity of chlordiazepoxide effect to that resulting from barbiturates or meprobamate. In such instances the frequency of background activity became slightly faster. In encephalomalacia, irregular high-voltage slow waves, localized in the right anterior temporal region, were reduced with concomitant clinical improvement following drug administration.

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Osaka, Japan

2343 Laine, T., Coupe, Baron, & Guittonneau. Expérience clinique de l'hexacyclonate de sodium (S. 186): Gevilon. [Clinical experience with hexacyclonate sodium (S 186): Gevilon.] *Annales Médico-Psychologiques*, 1962, 120, 1, 850.

Hexacyclonate was given to 60 cases of mental retardation, presenile states, involutional depression, oligophrenia, chronic schizophrenia and confusional states, in a dosage of 160 mg/day divided into 3 doses after meals. Some tendency towards convulsions appeared in predisposed subjects but the drug appears free of marked side effects. Most favorable indications were obtained in asthenia of the aged with an improvement in mental and social activity. In involutional depression its therapeutic activity could be termed remarkable.

[No address]

2344 Uytterschaut, M.P. Etude clinique d'un nouveau neuroleptique: le R. 1658 ou méthylpéridol. [Clinical study of a new neuroleptic: R 1658 or methylperidol.] *Annales Médico-Psychologiques*, 1962, 120, 2, 314.

Twenty-eight patients, refractory to other neuroleptics, were treated with an analogue of haloperidol, methylperidol (20-45 mg per day, even up to 150 mg/day). It is particularly effective in hebephrenia and catatonia. Tolerance was good and extrapyramidal symptoms mild; drug treatment was interrupted in only 1 case.

[No address]

2345 Sivadon, P., & Salinger, R. Etude clinique d'une nouvelle médication psychoactive en psychiatrie, le 8228 R.P. ou chlorhydrate de phényl-1-(pipéridyl-2')-1-acétoxy-1-méthane, thréo-lévogyre. [Clinical study of a new psychoactive drug used in psychiatry, RP 8228 or levophaceto-perane.] Annales Médico-Psychologiques, 1962, 120, 1, 824-832.

Levophaceto-perane (5-180 mg/day p.o.) was administered to 254 patients aged 16-80 years, about 77% of whom were engaged in various intellectual pursuits. In 211 cases, 5-40 mg/day was sufficient dosage. Duration of treatment was 1-3 months in 174 cases, 3-6 months in 55 cases and 6-12 months in 25 cases. Treatment was stopped in 25 cases due to intolerance and another 9 cases are difficult to interpret as improvement could not be directly ascribed to medication. Of the remaining 190 cases, 137 registered improvement, and 53 were failures. The number of failures and drug toxicity cases amounts to 46% of the total and improvements constitute 54%. Side effects consisted of insomnia, nervousness, mild excitation, digestive troubles, vertigo, palpitation and clonic spasms, all mild and suppressed by changes in dosage. Some epileptogenic tendency was noted, and the drug is contraindicated in such cases. When taken 1 hour before meals, it is also anorexigenic. It is indicated primarily for psychic asthenia, and is useful in neurotic depressions, reactive depressions and anxiety neuroses.

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2346 Schnetzler, J.P., & Lamand, J.C. Association systématique de la thioproperazine et de la thioridazine. A propos de 115 observations. [Systematic combination of thioproperazine and thioridazine. A report on 115 observations.] Annales Médico-Psychologiques, 1962, 120, 1, 123-133.

Thioridazine (50-600 mg/day) and thioproperazine (30-160 mg/day), with respective maintenance doses of 50-200 mg and 10-10 mg, were administered to 115 patients: 6 severe or epileptic oligophrenics, 6 with

dementias, 10 manics, 11 acute delirious psychotics, 27 with chronic delirium and 55 schizophrenics). The side effects of thioproperazine were remarkably attenuated by combination therapy. Only 2 excitomotor crises occurred, akinetic-hypertonic syndrome in only 16% of the cases, tremor in 24% and hyperkinetic syndrome in 6%. Daytime somnolence affected only 27%. Autonomic effects were mild and only occurred in 9%, while hypotension was encountered in 40%. Weight increases were noted in 53%, amenorrhea in 8 and galactorrhea in 15. A "down hill" syndrome was noted in a few aged persons, heralded by loss of weight. Cessation of therapy or dosage reduction is indicated for such persons.

Hopital psychiatrique
Saint-Egrève, France

2347 Lanternier, J. A propos d'un nouvel anti-convulsant l'alpha-éthyl-alpha-méthyl-succinimide. [A new anticonvulsant drug: alpha-ethyl-alpha-methyl-succinimide.] Pédiatrie, 1962, 17, 173-178.

Ethosuximide (alpha-ethyl-alpha-methyl-succinimide; 4-6 250 mg capsules/day) was administered to 44 children (12 petit mal with absences but without generalized crises, 14 with I.Q. varying from 75-100, including both generalized crises, absences of the petit mal type, and myoclonia. Seven of these patients were photosensitive and 18 remaining cases were encephalopaths) for 4-5 weeks. Concomitantly, diene medication was slowly decreased, but barbiturates were maintained. Of the petit mal cases, 11 showed complete clinical and EEG normality, while the 12th evidenced 50% improvement. Of the 14 centra-encephalics, 100% clinical improvement was observed along with 70-90% EEG improvement. Improvement was more rapid and complete in those who were not photosensitive. In the 18 encephalopaths considerable amelioration of clinical and electrical convulsions was noted. Side effects were generally slight, consisting of somnolence, vertigo and headaches at the start of treatment. In addition about half the children displayed anorexia, nausea, and gastric pains accompanied by vomiting and loss of weight.

However, these effects continued only 15-30 days and then stopped abruptly.

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2348 Jacob, Elizabeth, Marie, Claude, Thévenot, Jean-Pierre, & Dauxois, Françoise. Contribution à l'étude du 7843 R.P. (Majeptil) dans la schizophrénie. [Contribution to the study of RP 7843 (Majeptil) in schizophrenia.] *Annales Médico-Psychologiques*, 1962, 120, 1, 139-144.

Thiopropazine (Majeptil) was administered to 17 chronic schizophrenics, aged 25-55 years, with excellent results (possibility of discharge and adequate social readaptation) obtained in 3 cases, good results in 3, some improvement in 4, negligible results in 5, and 2 were aggravated. A battery of psychological tests was administered to 11 patients. These included Wechsler-Bellevue or Stanford-Binet intelligence tests, Heuyer-Baille Motor-Development tests, Seguintests, etc. Comparison of psychological test results and retests generally confirmed the modifications of schizophrenic structure mentioned above.

[No address]

2349 Fouks, Lainé, Mathis, Ferrant, Riou, & Bouchet. Note sur l'utilisation clinique de la dixyrazine. [Note on the clinical use of dixyrazine.] *Annales Médico-Psychologiques*, 1962, 120, 1, 392-399.

Dixyrazine is a methylated piperazine phenothiazine derivative. Clinical doses (35 mixed cases) were 50-100 mg/day for neuroses and mild depressions, and 150-200 mg/day for endogenous depressions and other psychoses. In depression, it was frequently combined with phenelzine, or imipramine. Side effects are generally mild, consisting of excito-motor troubles, slight hypotension, and diminished alertness. Neuroleptic psychomotor effects are frequently noted, but antiparkinsonian drugs (trihexyphenidyl and orphenadrine) generally alleviate the condition rapidly. Somnolence tends to occur in neurotic children and

psychotics, as well as some asthenics. Slight orthostatic hypotension is occasionally noted. Occasional increases in weight, aberrations of the menstrual cycle, galactorrhea, eosinophilia and leukopenia have been observed. EEG tracings disclosed with more regular alpha waves, 3 with more continuous alpha waves, 2 with slight increase in base voltage and 3 with a slightly flattened pattern; 14 cases showed no change and 8 gave typical somnolence tracings ensuing when the drug had been administered shortly before examination. The effect is mainly tranquilizing, anxiolytic and sedative, but the hallucinolytic and antipsychotic effects are feeble.

[No address]

2350 Savet, H. Incidence des traitements psychiatriques par l'iproniazide sur la dysménorrhée. [Repercussions on dysmenorrhea of psychiatric treatments with iproniazid.] *Annales Médico-Psychologiques*, 1962, 120, 1, 177-178.

Iproniazid was found beneficial in cases of spasmodic dysmenorrhea; 100 mg/day in the week preceding menstruation provides marked improvement. This has held true in the treatment of persons without any neuropathic signs. However the product should not be used systematically in these gynecological disorders because it should be handled with necessary precaution. Iproniazid appeared to have an activity at the level of uterine muscle, analogous to its activity on the myocardium.

[No address]

2351 Sutter, J.-M., Pascalis, G., & Girard J.Y. Centrophénoxine et collapsus cérébral [Centrophenoxine and cerebral collapsus.] *Annales Médico-Psychologiques*, 1962, 120, 1, 975.

A 30-year-old epileptic woman arrived in a coma and was treated rectally with centrophenoxine [dosage unspecified] and distilled water i.v. She regained normal consciousness in 36 hours after a confusional phase. Potassemia, initially low, also recovered. Centrophenoxine enriched

the gamut of drugs useful in the course of cerebral collapsus.

No address]

2352 Baroody, Naseeb B., Baroody, Waddy, & Mead, Walter R. Management of alcoholic withdrawal. Observation using chlordiazepoxide as chief tranquilizing agent. Journal of the South Carolina Medical Association, 1962, 58, 439-440.

Thirty-five consecutive alcoholic patients hospitalized during acute withdrawal were treated with chlordiazepoxide. At admission each patient was given 1000 ml of Baxter's No. 2 electrolyte solution containing vitamins, and 100 mg chlordiazepoxide i.m., sometimes with 50-100 mg promethazine or chlorpromazine i.m. The latter was given in instances of extreme agitation. For the 1st 24 hours chlordiazepoxide was continued i.m., 50-100 mg every 3-4 hours; after this dosage was continued as oral medication, maintained as long as psychomotor agitation existed. Agitation and excitation in most patients were controlled in the 1st 24 hours, and disorientation and hallucinations subsided promptly within 24-36 hours. Chlordiazepoxide led to resumption of normal eating for all within 72 hours. Results were generally satisfactory, but tremor did not respond well and persisted for several days despite treatment. No harmful side effects were observed.

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2353 Spira, Leo. Fluorine-induced endocrine disturbances in mental illness. Folia Psychiatrica et Neurologica Japonica, 1962, 17, 4-11.

Endocrine disturbances identical with those found in chronic fluorine poisoning and transferable to parathyroid and adrenal dysfunction were studied in 76 Japanese mental patients. These disturbances were represented by ectodermal lesions, particularly on the finger- and toenails, and brown skin pigmentation, including Riehl's melanosis. Twenty of these patients received anti-fluorine poisoning treatment [unspecified]

for 4 months. Treatment was considered completely successful in regard to skin discoloration, while no conclusion could be drawn with respect to the effect upon mental illness.

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2354 Gover, Douglas M. Thioridazine and chlorprothixene in the management of anxiety in tuberculous patients. American Review of Respiratory Diseases, 1962, 85, 587-590.

Thioridazine (25-300 mg/day p.o.), chlorprothixene (25-300 mg/day p.o.) or placebo was administered on a double-blind basis to 24 patients, aged 37-78 years, with anxiety states, for 90 days. Drugs were alternated every 30 days. Satisfactory to excellent results were obtained with thioridazine and chlorprothixene in 70 and 75% of the patients, respectively. Side effects for both active drugs included dry mouth, drowsiness, bitter taste, headache, vertigo, insomnia, etc. No correlation was observed between dosage and side effects or dosage and overall response. All patients had withdrawal symptoms or side effects from the placebo. A similar trial was conducted in 28 men with anxiety secondary to tuberculosis, utilizing thioridazine (average dose 135 mg/day p.o.), chlorprothixene (average dose 148 mg/day p.o.) and placebo. Good to excellent results occurred in 75% of the patients with both active drugs while all patients reacted to placebo within 48 hours with relapses into insomnia, restlessness and anxiety. Thioridazine was tested for 33 days and chlorprothixene for 39. Side effects were minimal.

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2355 Inose, Tadashi, Makino, Toshio, Sakai, Masao, Kobayashi, Hideo, Kajiwara, Akira, & Tsuda, Masatoshi. Use of dehydroepiandrosterone in psychiatric treatment. Preliminary report. Yokohama Medical Bulletin, 1962, 13, 37-45.

Dehydroepiandrosterone Δ^5 -androst-3- β -

al-17-one) was used in treatment of 104 psychiatric cases, mostly schizophrenia, neurosis and depression. The initial daily dose was 15-30 mg, in some cases up to 50 mg, in male patients; and from 6-20 mg, in some cases 30 mg, in females. Treatment was usually for 2 months but in some continued 6 months or more. No immediate changes were noted, but from 1-3 weeks responses occurred: 31 cases showed marked improvement, 16 mixed response, 37 no response and 20 cases were aggravated. Desirable changes were: brighter and milder attitude, more active and less withdrawn behavior, etc. Undesirable responses were: impulsiveness and aggressivity, including restlessness and increased erotic behavior. For 56 males, 16 were markedly improved, 8 had mixed responses, 21 no response and 11 were worse. For 48 females, responses were ibidem. 15, 8, 16 and 9. In schizophrenia, patients with immature personalities showed better response than others, while in depression those in a prolonged depressive state showed good responses. Physical changes such as masculinization, etc. were not noted. Urines were assayed for the β -fraction of 17-ketosteroids in 28 cases, and 18 of these showed a low β -fraction value, below 5% of the 17-ketosteroids.

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2356 Arruda, Elso. Observações clínicas com um análogo do clordiazepóxido—O RO 5-2807. [Clinical observations on an analog of chlorthalidazine—RO 5-2807.] O Hospital, 1962, 62, 937-955.

Twenty-five mixed cases, including 8 epileptics and 7 cases of anxiety, were treated with diazepam (RO 5-2807), 10 mg b.i.d. or t.i.d. Drowsiness sometimes necessitated the reduction to 10 mg/day. The compound is more active than chlorthalidazine. Besides somnolence, side effects included nausea, lassitude, cold sweating and rare visual disturbance. Tolerance is, in general, less than that for chlorthalidazine. Treatment lasted up to 4 months, usually 2-3 months. Results in 8 cases out of the 25 were considered good and in 9 fair. In

epilepsy, results were good in 5, average in 3 and negative in 1 with some EEG improvement, but without regular correlation between clinical and EEG findings.

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2357 Adams, Peter, Stephens, B.T., & Kilpatrick, G.S. Transaminase activity after codeine administration. Postgraduate Medical Journal, 1962, 38, 348-349.

Thirteen patients were studied before and after 2 grains of codeine i.m. Codeine administration did not affect SGOT or SGPT activity, except in one patient where there was an increase in transaminase activity. This evidence is in contradiction to that of Foulk and Fleischer (1957).

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2358 Favier, M., Ramel, P., & De Toffol M. Intérêt du méprobamate injectable en milieu psychiatrique. [The role of injectable meprobamate in the psychiatric milieu.] Lyon Médical, 1962, No. 48, 1125-1130.

Six alcoholics, 4 agitation, 4 psychotic, 9 neurosis with minor or moderate depression and 6 melancholia cases were treated with 1-4 i.m. injections of 400 mg meprobamate per day, later changing over to oral administration after the sedation of acute phenomena. The melancholia cases were treated with combined therapy—meprobamate with imipramine. Injectable meprobamate provided very satisfactory results in neurosis, minor or moderate depression and the acute manifestations of alcoholism. Some success was obtained in melancholia with the meprobamate-imipramine combination, but results were insufficient in major states with intense anxiety. Other types of psychoses remained unmodified.

[No address]

2359 Cox, Erwin M., & Loughheed, J.C.

pre- and postoperative use of prochlorperazine. Journal of the Tennessee State Medical Association, 1962, 55, 154-155.

Prochlorperazine was added to the routine preoperative medication, usually administered 1 hour before operation to 40 male and 56 female patients. Except for aged or debilitated patients who received 5 mg, all received i.m. 10 mg doses along with 50% dose of narcotics. Sixty out of the 96 patients entered surgery calm and relaxed, their apprehension minimal. Prochlorperazine tended to reduce the need for narcotics, afforded smooth induction of anesthesia, facilitated intubation and controlled emergence excitation. Of the 27 patients who vomited postoperatively, prochlorperazine achieved complete control in 25. Side effects were minimal; drowsiness occurred in 1 and hypotension in 8, 1 of whom were 50 years or older.

Department of Surgery
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Memphis, Tenn.

2360 Gerscovich, José. Sobre um caso de psicose esquizo-afetiva. "Até que ponto o ego do paciente está enfraquecido, e como fortalece-lo psicoterapeuticamente?" [On the case of schizoaffective psychosis; "At what point is the patient's ego weak and how can it be strengthened therapeutically?"] Revista Brasileira de Medicina, 1962, 19, 632-638.

A 28-year-old bisexual woman (IQ in the low 90's), divorced, suffering from schizoaffective psychosis, was studied in detail in relation to history, differential diagnosis and treatment. Treatment included 25 mg promethazine per day and 100-300 mg chlorpromazine t.i.d. Tests included WAIS, Rorschach, TAT, etc. Prognosis was reserved.

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2361 Portela, Jarbas M., Ribeiro Silva, Ivan, Ribeiro Silva, Antônio. Algumas implicações da terapêutica farmacológica da

ansiedade. (Nota sobre o uso da Flufenazina). [Some implications of the pharmacologic therapy of anxiety. (Note on the use of fluphenazine).] O Hospital, 1962, 61, 137-146.

Theoretical and practical implications of the role of fluphenazine in the suppression of anxiety are discussed and 7 cases are presented. Improvement in the suppression of anxiety and quarrelsomeness was obtained on a daily dosage of 1 mg fluphenazine/day, maintained over long periods, e.g., 6 months. This therapy aided in improving and maintaining psychotherapeutic measures.

Instituto Raul Soares
Belo Horizonte, Brazil

2362 Madalena, J. Caruso. Ensaio terapêutico com o clordiazepóxido no alcoolismo. [Therapeutic trial with chlordiazepoxide in alcoholism.] O Hospital, 1962, 62, 69-94.

Seventy-one male hospitalized patients in withdrawal were treated with chlordiazepoxide in 6 groups. Group A constituting 54.9% of the patients received only chlordiazepoxide; Group B constituting 15.4% received only chlorpromazine; Group C, 8.4%, was given chlordiazepoxide combined with chlorpromazine and Group F, 4.2%, received no treatment. All daily dosage was: 125 mg chlordiazepoxide and 150 mg chlorpromazine, in 3 divided doses; the maximal dose of the 1st drug was 200 mg per day and for chlorpromazine 300 mg per day. Duration of observation was 7-20 days. Chlordiazepoxide had higher efficiency than chlorpromazine and standard treatment. However, this drug does not seem indicated in alcoholics with a psychotic background in view of possible reactivation of psychotic disturbances.

Pavilhão São José
Universidade do Brasil
Rio de Janeiro, Brazil

2363 Hartocollis, Peter. Drunkenness and suggestion: an experiment with intravenous alcohol. Quarterly Journal of Studies on

Alcohol, 1962, 23, 376-389.

In a study of drunkenness and suggestion, as it is virtually impossible to mask alcohol in beverages, the i.v. route was chosen in experimentation with 15 subjects, all male psychiatric residents, aged 26-36 years. Their drinking habits were known and the group only included casual or moderate drinkers. Ethanol was injected, 1 ml/kg, as a 10% dilution in isotonic saline. This dose should produce a blood alcohol concentration of 0.1%, in the range regarded as putting an individual "under the influence." The infusion lasted about an hour. Emotion, speech and action were rated on a 5-point scale. A great deal of curiosity about the unknown agent was expressed, and more than a few made the right guess. Behavioral and subjective change was universal though not uniform. Subjects could look and feel drunk whether or not they knew or thought they were under the influence of alcohol. Behavior was difficult to evaluate; in most cases it changed towards elation and excitement followed by quieting, relaxation, sleep or stupor. Subjective reports included apprehension and bewilderment, parasthesia, peculiar taste, diplopia, dysarthria and disturbed proprioception, feelings of depersonalization, irresponsibility, euphoria and gregariousness, timelessness, fatigue and depression. More elation, aggression and boisterousness was noted when groups were tested compared to the testing of individuals.

VA Hospital
Topeka, Kan.

2364 Marx, H., & Krüger, H. Neue Gesichtspunkte in der neuroleptischen Behandlung akuter und chronischer Psychosen. Bericht über die klinische Prüfung neuer Thioxanthenderivate. [New viewpoints in the neuroleptic treatment of acute and chronic psychoses. Report on the clinical investigation of a new thioxanthene-derivative.] *Nervenarzt*, 1962, 10, 469-472.

One-hundred-and-twenty-one patients who were hospitalized were treated with chlorperphenthixene (Fifty-one were acutely and

70 chronically ill. The chronic patients had "psychic defects" and had been institutionalized for 3-25 years. In acute psychoses, various schizophrenic aspects could be favorably influenced. The effect was good also in cases of mixed psychoses, mania and exogenous psychoses. Conditions of excitation and tension, hallucinations, delusions and thought disturbances showed a tendency to improve. For agitated and excited patients drug treatment was initiated with 25 mg t.i.d. to 50 mg 5 times a day i.m. For all other cases 25-150 mg i.m. was sufficient. After 3-4 weeks of treatment all patients were maintained on 10-75 mg/day. Chemotherapy was combined with occupational therapy, bed rest was not advised. Physical side effects, especially at the beginning of treatment, were severe tiredness and an increased demand for sleep. Extrapyrimal symptoms were seen in 1/3 of all cases. Some hyperkinetic conditions were observed. Other physical side effects, such as a slight rise in body temperature, hypotonic disorders and the like, were not dependent on the dosage but on the individual constitution and the physical condition of the patient. All had previously been treated with ECT and/or insulin shock therapy, and with various neuroleptic agents. Chlorperphenthixene, given in low dosage, had an activating effect; it helped to increase initiative and promote the patient's contact with environment.

Westfälische Landeskrankenhaus
Gütersloh, Germany

2365 Broomfield, B. Acute intermittent porphyria treated with chlorpromazine. *Proceedings of the Royal Society of Medicine*, 1962, 55, 799-800.

A 27-year-old married woman showed a full picture of acute intermittent porphyria with pain, mental disturbance, diffuse abnormalities in the CNS, tachycardia and elevated blood pressure. An exploratory laparotomy was made with negative findings. Later the patient was deeply depressed and treated with amobarbital and trifluoperazine. Over a month later symptomatology changed towards paranoid schizophrenia. She was treated with 50 mg chlorpromazine

i.d. and 2 g chloral hydrate as a sedative, with strict bed rest. She was immediately relieved of muscle pain and gradually regained power, recovering, only later to suffer a relapse.

No address]

366 Vidal, M.G., Vidal, B., & Valéry, M.B. Essais cliniques du Ro 4-1575. [Clinical trials with Ro 4-1575.] *Annales Médico-Psychologiques*, 1962, 120, 1, 615-619.

Amitriptyline (Ro 4-1575) was used in the treatment of 36 female psychiatric cases. Ages were: 7, 20-40 years; 19, 40-60 years; and 10 patients 60-84 years. Usually dosage was 25 mg t.i.d., however in 3 patients the doses were 100, 125 and 150 mg/day, exceptionally 200 mg/day. Three out of 5 cases of melancholia were cured and 2 improved; in 3 cases of involuntional melancholia 2 were cured, while in 4 cases of senile melancholia 3 obtained remissions and 2 were improved. Results were transitory in another case of melancholia and a case of obsessional neurosis; these results were inferior to those from imipramine. In 2 cases of manic-depressive psychosis, amitriptyline did not appear stabilizing. In 4 cases of neurotic depression 3 improved and 1 was a complete failure. Lipothymia, visual disturbance and some vertigo were reported as side effects and transitory confusion occurred in 1 case.

No address]

367 Prigot, Aaron, Corbin, Eustace E., Maynard, Aubre de L., Roden, Thomas P., & Hjelt-Harvey, Inga. The treatment of delirium tremens with amino acids. Clinical and laboratory results with special reference to chromatographic determination of amino acids. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 390-410.

In poorly-fed alcoholics, the onset of delirium tremens often follows a period of stress such as trauma, acute infection or the challenge of a surgical procedure. A mixture of amino acids, metabolites and vitamins was concocted and administered

ed i.v. This solution contained: 2 g calcium glucuronate, 10 g sodium glutamate, 10 g cysteine, 10 g glycine, 10 g succinic acid, 0.5 g ascorbic acid and 1 g d-calcium pantothenate. The control group consisted of 51 cases and delirium tremens lasted 4.4 days while the treated group, 70 cases, had delirious attacks lasting 2 days. The amino acid treated subjects received a total of 9.025 mg (average 129 mg) of promazine and 720 cc (average 10 cc) of paraldehyde by way of adjunct therapy. In contrast, the control patients received a total of 1.297 cc (average 26 cc) of paraldehyde, 28 g (average 0.5 g) of barbiturates, 445 IU (average 91 U) of insulin, and 851 ounces (average 17 ounces) of whiskey. Free serum amino acids, the effect of stress on these acids, hepatic insufficiency and miscellaneous pathologies were assayed. Depletion of amino acids was characteristic of delirium tremens. The more serious the delirium, the greater the depletion of these essential blood elements. In further experimentation it was found that the amino acids sodium glutamate, arginine and arginine-glutamate and an amino acid sugar-n-acetyl-d-glucosamine-may be employed for the prevention or treatment of delirium tremens.

Division of Surgical Research
Department of Surgery
Harlem Hospital Center
New York, N.Y.

2368 Hill, Harris E., Haertzen, Charles A., & Davis, Howard. An MMPI factor analytic study of alcoholics, narcotic addicts and criminals. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 411-431.

MMPI profiles were obtained on institutionalized groups of alcoholics, narcotic addicts, and criminals, each sample being composed of 200 subjects. Application of the principal axes technique of factor analysis was made to the scale T-scores isolated 5 factors. Available factor analytic programs which were adapted to the IBM-650, accommodating approximately 45 variables, were used. Three of these were sufficiently well defined to produce predictable and stable personality configurations. The 1st factor, labeled "undifferentiated psycho-

path" and interpreted as indicating uncomplicated social deviance, was characterized by a single "spike" on the Psychopathic Deviate Scale. Small, statistically significant but nondiagnostic differences were found—criminals produced slightly greater loadings on this factor. Factor 2 was bipolar: The composite profile for the positive pole was much the same "double spike" (psychopathic deviate-hypomania) pattern as was found previously in narcotic addicts; it was labeled "primary psychopath." The negative pole was labeled "neurotic psychopath, depressed," since it showed considerable elevation on the neurotic triad, especially on depression, and on the Psychopathic Deviate Scale. While both factors showed strength in the 3 criterion groups, small but again nondiagnostic differences were found. The criminals were more numerous on the positive pole, the alcoholics more numerous on the negative pole, and the addicts were intermediate in factor loadings. Factors 3, 4 and 5 produced further evidence for the presence of classic psychopathologies, but with clear indications of social deviance (psychopathic deviate elevation) in all. Suggestions were made with regard to the adoption of certain modes of adaptation by the social deviant and for further research in the addictions.

Addiction Research Center, NIMH
Lexington, Ky.

2369 Helou, Horacio Antonio. Tratamiento combinado de hipnosis y trifluoperazina en diversas afecciones psicósomáticas. [Combined treatment of hypnosis and trifluoperazine in various psychosomatic diseases.] *Dña Médico*, 1962, 34, 951-952.

Eighty-three cases of neuroses, phobias and psychoneuroses were treated with hypnosis and trifluoperazine. Excellent results were obtained in 80% of the patients, who demonstrated marked and rapid improvement. Trifluoperazine (2-4 mg/day, in 2 or 3 doses) notably favored recovery, diminishing psychic tension and favoring adaptation to environment. Tolerance was excellent and the few side effects that were noted were transitory.

Hospital Policial "Bmé. Chukruca"
Buenos Aires, Argentina

2370 Haden, Hugh H., Jr., & Fowler, Raymond D., Jr. Prozine as an adjunct to psychotherapy with alcoholic outpatients in the withdrawal stage. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 442-448.

Prozine (200 mg meprobamate and 25 mg promazine tablets) was used in conjunction with psychotherapy in the treatment of alcoholic withdrawal symptoms in outpatient alcoholics. Seventy-nine out of 300 patients exhibited withdrawal symptoms when admitted and prozine was administered to 56; the other 23 received only vitamins. Of the Prozine-treated group, 39% continued in treatment compared with 13% of the untreated group. Patients admitted without withdrawal symptoms did not receive the drug and had a continuation rate of 30%, indicating that alcoholics admitted in withdrawal are more likely to continue in treatment than nonwithdrawn patients if given prozine. Patients were rated improved if they established partial or complete control over drinking in 6 months or more while making social gains in other areas. No withdrawn patient showed improvement who was not on Prozine whereas 11 on the drug improved. This improvement rate of 23% was higher than an improvement rate of 16% in all of the nonwithdrawn patients.

Birmingham Clinic
Alabama Commission on Alcohol
Birmingham, Ala.

2371 Soullairac, A., Schaub, Cl., & Morel, P. Action d'une butyrophénone-pipérazine (2028 MD) seule ou en association, sur les états d'agitation aiguë. [Action of a piperazine butyrophenone (MD 2028), alone or in combination, in states of acute agitation.] *Presse Médicale*, 1962, 70, 805-806.

Twenty patients were treated with MD 2028 (20 mg in 14 cases, 30 mg in 6) for acute agitational crises. Success was complete in 15 cases (75%), and partial in 2. Three failures were registered. In 3 cases, reserpine (3-6 mg) was added to the regimen and in 3 other cases barbiturates were added. These combinations appeared favorable, allowing a lower dosage to be used. Side effects were minimal consisting of nausea

vomiting and parasthesias in rare instances.

Centre psychiatrique Sainte-Anne
Paris, France

2372 Saucedo Galindo, Mario, Montaña Castellanos, Rodolfo, & Uribe Amador, J. Rafael. Recuperación acelerada de los estados depresivos con la 2-hidroximetilene 17- α -metil-androstan-17 β -ol-3-one (oximetolona), asociada a medicamentos psicoanalepticos en enfermos seniles. [Accelerated recovery from depressive states with 2-hydroxymethylene 17- α -methyl-androstan-17 β -ol-3-one (oxymethylone), combined with psychoanaleptic drugs in senile patients.] Prensa Médica Mexicana, 1962, 2, 107-110.

Ten cases of depression in older persons, aged 50-65 years, were treated with oxymethylone (2.5-10 mg/day) combined with psychoanaleptics. The psychoanaleptics (mg per day) were: iproniazid (100-150), imipramine (50-100), perphenazine (4-5) and trifluoperazine (2-4). Clinical ratings were made weekly and weight was assessed periodically. Ninety percent recovered rapidly, e.g., 32 days. Increase in body weight (0.4-8 kg) followed clinical improvement.

Departamento de Neurología y Psiquiatría
Universidad Autónoma de Guadalajara
Guadalajara, Mexico

2373 Huguet, P.E., Girard, M.J., Cauquil, G. & Sanquerpogu. Action des cures prolongées de thioridazine dans les psychoses chroniques rebelles et dans certaines psychoses aiguës. [Action of prolonged thioridazine therapy in refractory chronic psychoses, and in certain acute psychoses.] Annales Médico-Psychologiques, 1962, 120, 2, 296-303.

Thioridazine (50-1000 mg/day p.o.) was administered to 100 patients with acute and chronic psychosis. Mean dosages were 300-600 mg for acute cases and 300-400 mg for chronic cases. Side effects were slight, consisting of occasional cardiovascular hypotension, and minor parkinsonian symptoms. Considerable endocrine disturb-

ance was noted: galactorrhea, oligomenorrhea and amenorrhea. A tendency to gain weight was troublesome, particularly to female patients. The effect of the drug was excellent on 13 acute neurotic depressions, 7 of whom were able to return to work, while considerable improvement was noted in the remaining 6. Partial success was recorded with 7 acute melancholics. Of 28 schizophrenics, 15 failures were recorded, and 13 moderate to good improvements. Only 3 failures, and 16 partial to total successes were noted in 19 chronic delirium cases. Out of 11 feeble minded patients, 3 were failures and 8 evidenced partial to considerable improvement; 8 oligophrenics were unresponsive, revealing only 2 who improved. Treatment was successful in 40%. Thioridazine is indicated in all acute states, in systematic deliria, and comprehensive depressions.

Hopital,
Sotteville-les Rouen, France

2374 Girard, J.P. Essais cliniques d'un nouvel antiallergique, l'homochlorcyclizine. Effets sur l'élimination urinaire du métabolite de la sérotonine. [Clinical trials of a new antiallergic, homochlorcyclizine. Effects on the urinary excretion of the metabolite of serotonin.] Therapeutische Umschau, 1962, 19, 50-53.

Forty-three cases of allergy, including asthma, drug dermatocytosis, ulcerative colitis, etc. were treated with homochlorcyclizine (100 mg p.o. and 60 mg parenterally; once it was administered as an aerosol). Duration of treatment was from some days to a month. Urinary 5HIAA was assayed by the technique of Udenfriend et al. Fourteen showed good improvement and 16 average improvement. Side effects were nausea, drowsiness, anorexia and headaches. Tolerance was excellent. In asthma cases, homochlorcyclizine caused a slight increase in urinary 5HIAA, while in rheumatism 5HIAA excretion was lessened.

Clinique universitaire de médecine interne
de Genève
Geneva, Switzerland

2375 Bitter, Tobias. Tratamento das cefaléias pós traumáticas com um antagonista da serotonina. [Treatment of posttraumatic headaches with a serotonin antagonist.] *Revista Brasileira de Medicina*, 1962, 19, 543-544.

Methysergide was used i.m. in 10 cases of posttraumatic headache at a dose of 1 mg every 8 hours and at half this dose for children (2). Placebos were not used but the patients did not know the nature of the medication; evaluation was made by soliciting information daily. Methysergide provided relief of pain from headaches without the production of side effects.

Departamento de Neurologia
Santa Casa de Misericórdia
Rio de Janeiro, Brazil

2376 Puech, J., Robin, Ch., Richet, L., & Tetart, A. Effets du N. benzyl beta chlorpropionamide (Posedrine) sur les anomalies caractérielles de sujets épileptiques ou présentant des perturbations du tracé E.E.G. [The effects of N-benzyl- β -chlorpropionamide (Posedrine) on character disorders in epileptic subjects or those presenting abnormal EEG's] *Presse Médicale*, 1962, 70, 1015-1018.

Thirty-six cases, 31 below 18 years of age and 5 adults, showing character disorders, behavioral disorders or psychotic abnormalities were treated with 4-9 tablets of beclamide (Posedrine) per day. Duration of treatment was 3-22 months. There were 14 cases of epilepsy. Fifteen out of the 36 cases improved markedly (41%) and 7 (19%) improved slightly, i.e., 60% of the cases improved. The number of epileptic seizures was decreased but mental status rarely improved. In nonepileptics, EEG's were improved, particularly those demonstrating a tendency toward epilepsy.

[No address]

2377 Schwaar, Robert. Essais de tolérance de la méphénoxalone (OM-518) sur le tractus digestif. [Tolerance trial of mephenoxalone (OM-518) on the digestive tract.] *Therapeutische Umschau*, 1962, 19, 165-168.

Thirty-six cases of gastric or duodenal ulcer with complications were treated with mephenoxalone (e.g., 2 1 g tablets per day). In general, the agent was efficacious from the standpoint of reducing psychotension, anxiety and functional digestive disorders, pure or with a psychosomatic component. Also, tolerance was perfect in relation to gastric, hepatic or renal symptoms.

[No address]

2378 Bueno, Ursulina Penteado, & Capp, Antonio B. Resultados clínicos conseguidos ao emprêgo de um novo psicotônico em menores oligofrênicos e epilépticos oligofrênicos. [Clinical results following the use of a new psychotonic in oligophrenic-epileptic and oligophrenic children.] *O Hospital*, 1962, 62, 1003-1017.

Eighty-four patients including retarded children, imbeciles and idiots with and without epilepsy were treated with 2 5 mg tablets of levophacetoperane (RP 8228) daily for 5 days, followed by 3, then 4 tablets, etc. until by the 26-30th day doses of 6 tablets daily were given which is considered optimal. The total dose per patient was 120 5 mg tablets and the duration of treatment was 30 days. Barbiturates were also administered to the 41 epileptic patients. Only 1 patient showed side effects—allergy, possibly not attributable to the medication. The drug does not seem to be contraindicated in epilepsy and anxiety. Of the 84 patients, 41.67% showed considerable improvement, 34.52% improved, 22.62% were unaltered and 1.19% (1 case) worsened.

Divisão de Psicopatologia Infantil
Hospital de Juqueri
Belo Horizonte, Brazil

2379 Dos Santos, Oswaldo. Sobre o uso de uma nova fenotiazina, a flufenazina, em esquizofrênicos com várias internações e já submetidos a outros tratamentos. [On the use of a new phenothiazine, fluphenazine, in previously hospitalized schizophrenics submitted to other treatments.] *Revista Brasileira de Medicina*, 1962, 19, 421-428.

Three paranoid, 3 catatonic and 1 hebephrenic-catatonic schizophrenic women who were previously exposed to various therapies were treated with fluphenazine. At the beginning dosage was 1-2.5 mg, usually reaching 15-20 mg in most patients; 45 mg per day was given to 1 patient. Duration of treatment was approximately 60 days. Extrapyramidal reactions set in at doses about 15 mg/day, easily controlled with antiparkinsonian medication or by reducing the dose. Orthostatic hypotension occurred

in 1 case. Of the 7 cases, 5 obtained excellent results, 1 good results and the other was unaltered.

Hospital Pedro II (S.N.D.M.)
Rio de Janeiro, Brazil

See also 2240, 2241, 2262, 2265, 2269, 2382, 2463, 2489, 2512, 2523, 2527.

2380 Gardner, Alvin F., Gross, Sheldon G., & Wynne, Larry E. An investigation of gingival hyperplasia resulting from diphenylhydantoin sodium therapy in seventy-seven mentally-retarded patients. *Experimental Medicine and Surgery*, 1962, 20, 133-158.

An extensive review of the literature on gingival hyperplasia due to diphenylhydantoin therapy preceded an investigation of 77 mentally retarded patients who received diphenylhydantoin (7.5 grains/day). Some degree of gingival hyperplasia was shown by 78%, spastic patients exhibiting a higher percentage than others. Gingival hyperplasia showed no sex predilection and was more prevalent among those under 30 years-of-age. Neither dosage increase nor duration of therapy affected the degree of hyperplasia, and the prodromal period had to elapse before hyperplasia reached its peak. Degrees I and II were the most prevalent forms of hyperplasia, and the most severe, Degree III, was least prevalent. While patients with relatively normal occlusion had the greatest incidence of hyperplasia, the more serious the malocclusion the greater the degree of hyperplasia. Frequent proper, adequate brushing may decrease the degree of hyperplasia, but it will not eliminate it. Although calculus does not appear to affect the degree or act as a predisposing factor, it may influence an already established condition. No definite cure is known, and the etiology remains obscure.

Department of Pathology
Baltimore College of Dental Surgery
Dental School
University of Maryland
Baltimore 1, Md.

2381 Périn, M., Conte, Gamerman, J., & Salet, J. Hépatite aiguë mortelle au cours d'un traitement par l'iproniazide (marsilid). [Fatal acute hepatitis during iproniazid therapy (Marsilid).] *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, 1962, 113, 13-20.

A female patient, aged 49 years, with severe jaundice and symptoms resembling those of choledocic lithiasis died within 48 hours after admission, despite treatment with antibiotics, hydrocortisone, arginine, vita-

mins and liver extracts. Autopsy revealed necroticizing hepatitis, which had developed over a 3-week period with hypertrophy of the hepatic cells. The patient had been under treatment for a chronic depression most recently with iproniazid, which had been instituted shortly before the jaundice had appeared. Clinically, the case is similar to Rokitsky's disease, and a viral origin cannot be completely obviated. Iproniazid may have been responsible since the presiding psychiatrist had observed 2 other cases of icterus (benign) out of 50 patients so treated. Morbidity rates indicate that icterus in iproniazid patients is possible, its frequency, (1 in 2000) being about double that of the population at large.

[No address]

2382 Buisson, M., Collier, G., Armand-Laroche, J. L., Szymonowicz, R., & Bouchard, J. M. A propos de crises d'épilepsie survenues au cours de traitements par le tartrate d'alimémazine (6549 R.P.) ou théralène. [Epileptic seizures occurring during treatments with alimemazine tartrate (RP 6549) or Theralene.] *Annales Médico-Psychologiques*, 1962, 120, 1, 775-781; discussion 781-782.

Of the 30 patients who had received alimemazine (mean dose 100 mg t.i.d.) 8 experienced epileptic crises which ceased with suspension of alimemazine therapy. Vitamin B deficiency, secondary to isoniazid therapy is believed responsible for the rapid onset of crises in 2 of these patients. Another 2 had a history of epilepsy, but convulsive phenomena had never occurred in the hospital prior to theralene administration. Another 2 had a family history of encephalopathy, but 2 had no pathological antecedents capable of explaining the crises, and their EEG's were within normal limits. The above figures refer to women only since none of the 38 male patients on the drug experienced these crises. Alimemazine is currently being continued, but phenobarbital (50 mg/day) is being administered as prophylaxis. No further crises have been noted.

[No address]

2383 Frankland, A.W. Skin testing and desensitization to drugs. Proceedings of the Royal Society of Medicine, 1962, 55, 46-48.

Patch testing has frequently been used to detect drug sensitivity to various allergens. It is imperative to differentiate among true allergic reactions, irritant reactions and nonspecific false positive reactions. Sunlight has been known to act nonspecifically in atopic individuals who exhibit no abnormal response to tests for photosensitivity, such as a woman treated with promethazine who developed hemorrhagic vascular eczema on her hands along with photosensitivity. The immediate type wheal response and passive transfer tests for demonstrating Prausnitz-Küstner antibodies are very rarely of value in finding causal agents in allergic drug reactions. Desensitization procedures, although arduous, must sometimes be undertaken.

[No address]

2384 French Devitt, R.E., & Kenny, Shelia. Thalidomide and congenital abnormalities. Lancet, 1962, No. 7226, 430.

Within 8 months 3 cases of phocomelia, 2 with duodenojejunal stenosis, were observed in South Down and Armagh, a region where no such case had arisen for at least 8 years. Further consultation revealed that thalidomide (100 mg/day) had been ingested by the 3 mothers, 2 of whom took the drug from the 5th to the 13th week of pregnancy, while the 3rd took it throughout pregnancy.

South Down Hospital Group
Newry, County Down
Great Britain

2385 Schaefer, Suzanne. Toxicity from drug overdosage in an eleven-year-old boy. Clinical Pediatrics, 1962, 1, 103-104.

An 11-year-old boy ingested 17 tablets of chlordiazepoxide (425 mg) and 1-1/2 gr. of secobarbital after which he rapidly became deeply comatose with pinpoint pupils, absent deep tendon reflexes and a weak

pulse. At the time of admission there was no suspicion of chlordiazepoxide intoxication, and general supportive therapy included caffeine (3-1/2 grains by i.v. drip), stomach aspiration, i.v. glucose solutions, penicillin and chloromycetin. Chlordiazepoxide was not detected by laboratory tests and the diagnosis was suggested only by questioning the family. Pentetrazol (7 cc i.v.) injections did not help. However, 36 hours after chlordiazepoxide ingestion the boy regained consciousness. Within 3 days he was able to be discharged.

[No address]

2386 Pick, Edgar. Adrenaline and schizophrenia. Lancet, 1962, No. 7227, 487.

A 50-year-old man who received a prophylactic tetanus antitoxin experienced an immediate anaphylactic reaction with severe hypotension, convulsions and loss of consciousness. Epinephrine (1 mg s.c. adrenaline) resulted in rapid recovery. However, shortly after recovery he became incredibly suspicious and anxious. Within 1 hour his behavior was normal and he had slight amnesia for his previous reaction. This paranoid reaction to an epinephrine injection apparently constituted an emotionally charged response in a predisposed person.

[No address]

2387 Clemmesen, C., Myschetzky, A. and Lassen, N.A. Forced diuresis in treatment of severe salicylate poisoning. Lancet, No. 7221, 1962, 162.

Forced diuresis was used in a series of 31 consecutive cases of severe salicylate poisoning, with only 1 fatality (recurrence of cerebrovascular disease in a patient with recent apoplexy). Few complications were encountered. Diuresis is being utilized in Denmark to treat severe meprobamate poisoning. Essential adjunctive therapy includes symptomatic supportive treatment counteracting respiratory, circulatory and infectious complications. Proper assessment of the efficacy of diuretic treatment in salicylate intoxication is predicted upon the determination of blood and urinary drug

Department of Psychiatry
University of Leeds
Leeds 2, Great Britain

2388 Sezgin, Ziya, Bosworth, David, & Frost, Harold M. Effect of Marsilid on diaphyseal lamellar rabbit bone. *Henry Ford Hospital Medical Bulletin*, 1962, 10, 209-216.

Experimentation in rabbits was prompted by the observation that iproniazid-(Marsilid) treated-patients appear to show abnormal bone qualities at the operating table. Eight out of 10 rabbits received iproniazid (10 mg/kg/day by stomach tube for 3 months, while 2 acted as controls to determine the effect of iproniazid on diaphyseal lamellar bone. All were healthy when sacrificed at 6 months of age with no evidence of liver damage. Sections of the tibia and femur from iproniazid-treated animals revealed considerable micropetrosis, a decrease in internal cortical remodeling and an increase in the number of necrosis in osteocytes. Then, 52 rabbits received tetracycline p.o. by gavage for 2 weeks followed by 2 weeks of abstinence and another 2 weeks of tetracycline treatment. Of this group, 26 also received iproniazid, 3 mg/kg/day for 6 weeks. Iproniazid-treated animals showed retardation of internal bone remodeling, and both groups indicated that tetracycline produced an unequivocal decrease in osteoid formation and rate of mineralization. Iproniazid decreased the rate of circumferential lamellar apposition. Oral tetracycline labeling proved to be completely unsatisfactory in labeling rabbit bone. In a 3rd experiment, 15 rabbits received tetracycline labels, 200 mg/kg i.p. on the 1st day of 3 successive weeks. Iproniazid (25 mg/kg/day) was given to 6 animals for 1 week and cortisone (50 mg/kg/day) was given to 3 animals for 1 week. Two of the iproniazid-treated animals died during the experiment and the remainder were sacrificed 1-9 days after termination. Gross and histological liver damage was observed in the 2 who died prematurely. Bone sections in the remaining iproniazid-treated animals revealed an increase in osteocyte death, little active periosteal bone formation, few osteoid seams and little fuchsin-permeable bone. Those sacrificed a week or more after the experiment manifested very active per-

ioseal new bone formation. Cortisone-treated animals revealed almost total arrest of new bone formation. Cortisone-treated animals sacrificed well after the experiment showed, after a week or so, greatly augmented new bone formation (rebound) with very active periosteal appositional activity. The effects of iproniazid may have resulted from an endogenous increase in cortisone secretion accruing from experimental stress.

[No address]

2389 Moore, Henry W. Toxicity of phenothiazine tranquilizers. *Journal of the South Carolina Medical Association*, 1962, 58, 485-486.

A severely dehydrated 12-year-old girl received prochlorperazine (10 mg every 4 hours) suppositories for vomiting and diarrhea. Vomiting ceased, but bizarre facial contortions, oculogyric crisis, trismus, hypertonic extremities and various other extrapyramidal symptoms were manifested. Side effects disappeared after 12 hours of forced i.v. fluids to correct dehydration.

Columbia, S.C.

2390 Helmchen, H., & Hippus, H. Unerwartete neurologische Begleiterscheinungen der Pharmakotherapie von Psychosen. (Prinzipielle Bemerkungen anhand kasuistischer Beispiele). [Unexpected neurologic symptoms during treatment of psychoses with psychopharmacologic drugs.] In: Kranz, H., & Heinrich, K. [Eds.] *Neurolepsy und Schizophrenie*. [Neurolepsy and Schizophrenia] Stuttgart: Georg Thieme Verlag, 1962, 77-84; discussion 84-87.

One manic-depressive and 2 paranoid patients were treated with orphenadrine (2 tablets i.d.), and with perazine (300-550 mg i.d.). During this treatment, Oppenheim, Gordon and Babinski reflexes developed with orphenadrine, and ataxia of upper and lower extremities, spastic paralysis of both lower extremities and fecal and urinary incontinence on perazine. All of these symptoms disappeared after cessation of treatment. In all cases very slight neuro-

logical disturbances were noted at the time of admission which developed during treatment into the above described symptoms. A latent and minor pathologic disposition of the CNS may have been activated by the drug administration and may have produced

the well-defined reversible symptoms.

[No address]

See also 2245, 2247, 2272, 2298, 2341, 2415, 2444, 2470.

2391 Leikola, Anto. Influence of stress on alcohol intoxication in rats. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 369-375.

Four-month-old rats of both sexes were stressed by forcing them to swim in a large cask of water at 34-36°C. They soon learned how to float without effort, and therefore an 8 g weight was attached to their tails so that they had to swim actively—generally 10 minutes exhausted them. Fasted rats were administered a 30% ethanol solution immediately or 30 minutes before swimming, and in 1 experiment alcohol was given i.p. as a 10% solution. The doses were 3.6, 4.5 and 5.0 mg/g p.o. and 2 mg/g i.p. Levels of intoxication were tested on an inclined plane. The intoxication level of stressed rats was much lower than that of unstressed controls. When alcohol was administered orally, the blood alcohol also was lower in the stressed animal; after i.p. injection blood alcohol level was the same in stressed and unstressed rats. However the stressed rats were less intoxicated than controls with corresponding blood alcohol levels. With i.p. administration at the same blood alcohol level 90 minutes after the injection, the degree of intoxication in stressed animals was only about 40% of that in controls. Intoxicated rats could recover when subjected to swimming tests, though this was transitory. No convincing explanation for the intoxication—diminishing effect of stress can yet be given. A possible explanation is the influence of adrenal hormones released during stress.

Research Laboratories of the State
Alcohol Monopoly
Helsinki, Finland

2392 Masserman, Jules H. Drugs, brain and behavior; an experimental approach to experimental psychoses. *Journal of Neuropsychiatry*, 1962, 3, S104-S113.

Following preliminary control observations for 2-10 months 152 cats and 48 monkeys (African vervet and Mangebey, American spider and rhesus) were trained to respond to a specific stimuli by pressing 1 of 2 reward levers. Experimental neuroses were

evoked through an adaptational impasse between previously learned pattern and concurrently induced fear of a disruptive traumatic experience. Treatment constituted a variety of techniques: satiation of 1 conflictful need, change of environment, forced solution of adaptational impasse, group examples of "normal" behavior, retraining, drug administration, cerebral surgery, and/or various forms of shock therapy. Results indicated that normal or neurotic animals with total cerebral capacities diffusely impaired by EST or locally impaired by bilateral lobotomy, thalamotomy or amygdaloidectomy were more liable to have their adaptive capacities further disorganized by alcohol, morphine, barbiturates or repeated psychological traumas than animals with intact nervous systems. Despite induction of lethargy and ataxia the barbiturates offered, particularly in feline subjects, the greatest amelioration of neurotic symptoms, producing a minimum of undesirable side effects and offering a fair degree of protection against intercurrent traumatic experiences. Alcohol ranked 2nd to barbiturates. Reserpine, chlorpromazine and meprobamate produced less immediate relief from experimentally induced neurotic or psychotic behavior and induced a greater number of sympathetic and motor complications. No drug could obviate the effects of prolonged adaptational conflict. Some contingencies which could alter, reverse or abolish the usual pharmacologic action of the drug included: external environment, social milieu, internal environment and administration. Difficulties in control were elucidated, i.e., variability in handling of animals, discrepancies in observations and grading, etc., as well as the difficulty in relating animal behavior to that of human beings.

Northwestern University
School of Medicine
Chicago, Ill.

2393 Myers, Arlo K. Alcohol choice in Wistar and G-4 rats as a function of environmental temperature and alcohol concentration. *Journal of Comparative and Physiological Psychology*, 1962, 55, 606-609.

Forty Wistar and 40 G-4 rats were each

Given the choice of an ethyl alcohol solution or water for 22 hours. Drinking tests were carried out under controlled temperature and humidity conditions. Different groups of rats were tested in all combinations of 3 experimental variables: Wistar versus G-4 strain, 18° versus 27°C drinking test cage temperature and 5 different percentage by volume concentrations (1.25-10.00%) of alcohol versus water in the selection test. At all combinations and temperatures, G-4 rats selected more alcohol than Wistar rats; at 27°C both strains drank more alcohol than at 18°, and all groups (except the Wistar rats at 18°C) showed a greater mean intake of alcohol solution than water. Wistar rats at 18°C gave no evidence of alcohol preference at any concentration. The finding that alcohol selection was clearly related to environmental temperature indicates further research is needed to uncover the mechanism involved, and emphasizes the need for well-controlled temperature conditions in alcohol selection tests.

Division of Social Sciences
University of California
Riverside, Calif.

2394 Rahmann, H. Einfluss des Chlorpromazins auf das Gedächtnis von Goldhamstern. [The influence of chlorpromazine on memory in golden hamsters.] *Pflüger's Archiv*, 1962, 275, 95-106.

The influence of chlorpromazine (0.5, 1 and 2 mg/kg s.c.) on discrimination learning, retention and transposition ability was tested after methods developed by Rensch and Rahmann (1960) in golden hamsters. Three groups of hamsters were trained to discriminate 2 simple visual patterns while given injections. Controls received an equivalent injection of saline. During conditioning the 3 chlorpromazine groups showed significantly impaired function in relation to controls. Retention was tested 14 days after the criterion had been learned and then at 10 day intervals. The memory of all chlorpromazine-treated animals was very poor in comparison to controls. In relation to transposition ability (ability to recognize the visually learned pattern in a changed form), hamsters which received

chlorpromazine during conditioning and retraining, but not before the transposition test, showed a much more impaired performance than controls. Chlorpromazine acts as a CNS sedative, reducing the intensity of association formed during conditioning so that impaired memory and transposition ability results.

Zoologische Institut
Universität Münster
Münster, Germany

2395 Rodgers, David A., & McClearn, Gerald E. Mouse strain differences in preference for various concentrations of alcohol. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 26-33.

Tap-water and 6 concentrations of alcohol, 2.5-15%, in 2.5% increments were given ad lib to C57BL, BALB/c, C3H/2 and ACrgl/3 strains of mice, approximately a year in age. The amount of liquid consumed from each cylinder was recorded daily for a period of 3 weeks. The C57BL strain showed the highest preference for the 12.5% solution and a progressive increase over the 3 weeks in the proportional amount of alcohol consumed. The C3H/2 strain showed a progressive shift in preference from lower concentrations during the 1st 2 weeks to a pronounced peak preference for 10% alcohol during the 3rd week. The BALB/c and A/3 strains tended to avoid all concentrations of alcohol, preferring water. This preference for water, initially pronounced, tended to increase. Strain differences in change in alcohol consumption from the 1st to 3rd week were related to initial strain differences in preference. Alcohol preference of mice is suggested as influenced by a multiple-allele or a multiple-gene system or both.

Cancer Research Genetics Laboratory
University of California
Berkeley, Calif.

2396 Purdy, Maud B., & Lee, Jordan G. The effect of restricted food intake, thiamin deficiency and riboflavin deficiency on the voluntary consumption of ethanol

by the albino rat. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 549-556.

Paired litter-mate rats were allowed a choice between water and 15% ethanol. They were fed a normal diet ad lib. for 6 days to establish normal intakes. One member of each pair was then shifted to a ration devoid of thiamine (11 pairs) or riboflavin (8 pairs) and paired feeding was begun. As food intake decreased, the level of vitamin intake was maintained at levels established during the initial feeding period. After 24 days on the thiamine experiment, or 56 days on the riboflavin experiment, each animal was given 6 g per day of the complete ration for a 5-day period, then returned to ad lib. consumption of the complete ration for 20 days. Significant mean intrapair increases in alcohol intake produced by lack of thiamine or riboflavin were not evident. Deficient and paired nondeficient groups increased their alcohol consumption above the norms established during the initial feeding period. These differences were significant only in the males paired with riboflavin-deficient males, females paired with thiamine-deficient females and the thiamine-deficient females. Alcohol intake increased when the previously missing vitamin was added and food intake limited. These increases held true above the final 5 days of depletion in previously thiamine-deficient but not in riboflavin-deficient animals. Ad lib. feeding of the complete ration restored intakes to the initial value. Increases in alcohol intake were due to decreased food intake resulting in tissue loss, and not to thiamine or riboflavin deficiency. The thiamine or riboflavin deficient rat is less able to utilize alcohol and therefore consumes less than when given the vitamin with restricted food intake.

Department of Chemistry
Louisiana State University
Baton Rouge, La.

2397 Feuer, G., & Broadhurst, P.L. Thyroid function in rats selectively bred for emotional elimination. III. Behavioral and physiological changes after treatment with drugs acting on the thyroid. *Journal of Endocrinology*, 1962, 24, 385-396.

Sixty rats from the Maudsley Reactive and Non-reactive strains bred for emotional defecation were given either propylthiouracil (PTU), TH or potassium iodide. Both defecation and ambulation (Hall's test of emotionality, revised and standardized) scores were used. PTU (0.1% at ca. 10 mg per day in drinking water) treated Reactive high-defecating rats increased defecation scores significantly while the ambulation score decreased slightly; in the Non-reactive low-defecating rat, no significant changes occurred in defecation scores. After TSH i.p. injection (0.1 ml twice weekly of 1 IU), behavioral scores did not change significantly, although defecation scores were decreased and the ambulation scores increased in the majority of cases. No significant changes were observed with potassium iodide administration (approximately 0.5 mg per day of a 0.001 M dilution in drinking water). Differences in adrenal weight were found, the gland significantly larger in the high defecating strain than in the low one. The ovaries of the high defecating females were significantly smaller than those of the low defecating ones. No marked difference was found in the pituitary and testes weight. Kidney weight was significantly lower in the high defecating strain. PTU and TSH treatment altered the size of the thyroids, the serum protein bound iodine and the adrenals and the kidney weight was affected. While it is not known whether behavioral differences were caused by direct effect on defecation by thyroid hormones or direct hormonal effect on nerve cells, the differences are probably related to pituitary regulation of TH production.

Department of Biochemistry
Institute of Psychiatry
University of London
London, Great Britain

2398 Adey, W. Ross, Bell, Frederick R., & Dennis, Barbara J. Effects of LSD-25, psilocybin, and psilocin on temporal lobe EEG patterns and learned behavior in the cat. *Neurology*, 1962, 12, 591-602.

Eighteen cats were implanted with electrodes and trained in 2 situations: food reward on a visual cue in a T-maze

and delayed response training for a concealed food reward. The LSD was given in i.p. doses of 25-100 μ g/kg, 0.25-1 mg per kg psilocybin, 0.25-1 mg/kg psilocin. After LSD, cats adopted a wide-based "kangaroo" position with the tail extended, and exhibited staring, head shaking, and sprawling with claws extended. There was a loss of normal affective responses. These seizure-like episodes were seen in EEG records in a quiet environment; they were maximal in amplitude and were longest in duration in the dorsal hippocampal and entorhinal cortex, appearing variably in the thalamus and in the mid-brain reticular formation. These seizures seemed critically dependent on reduction of visual and auditory sensory influences. At higher LSD doses, seizures persisted in a well-lit environment and disrupted a delayed response when the seizure episode encroached on the period when a discriminative performance was required. Unlike visual and auditory stimuli, the ingestion of food during the action of LSD was frequently associated with wave and wave-and-spike seizure activity, confined in some instances to hippocampal and amygdaloid systems. Tolerance to LSD appeared with doses repeated at more frequent intervals than 7-10 days. Psilocybin and psilocin resembled LSD in their general effects but did differ in both the brevity of their action and in the frequent occurrence of severe autonomic reactions. Included among these severe autonomic reactions were vomiting, micturition, and finally, pupillary dilatation. The relationship of all of these findings to physiologic mechanisms in the memory trace and to the various problems of sensory deprivation is discussed.

Brain Research Institute
Department of Anatomy
University of California
Los Angeles, Calif.

2399 Bignami, Giorgio. Influenza della l-tiroxina ed elmetilitiouracile sul condizionamento e la ritenzione nel ratto. [Influence of l-thyroxine and methylthiouracil on conditioning and memory in the rat.] *Rendiconti Istituto Superiore di Sanità*, 1962, 25, 165-175.

CAR's (shuttling response) were developed in male Wistar rats in a modified Warner automatic programmed shuttle cage. Four groups were developed: controls, 0.2 mg/kg l-thyroxine s.c., 0.1% methylthiouracil in the drinking water for 14 days and methylthiouracil plus thyroxine for 14 days. Hypothyroidism while not affecting acquisition during any day's trials, retards retention as measured on the early trials of successive daily tests. Injections of l-thyroxine did not significantly modify the behavior of otherwise treated rats. In hypothyroid rats, however, injections of thyroxine not only eliminated the impairing effects of the deficiency, but seemed to facilitate both acquisition and retention in early trials in comparison to control rats.

Laboratori di Chimica Terapeutica
Istituto Superiore di Sanità
Rome, Italy

2400 Latané, Bibb, & Schachter, Stanley. Adrenalin and avoidance learning. *Journal of Comparative and Physiological Psychology*, 1962, 55, 369-372.

Fifty naive male rats were trained in a modified Miller-Mowrer shuttle box. After each injection the rat was allowed to explore the box with the guillotine door lifted in order to check the possibility that epinephrine (adrenalin) may influence activity level and thus artifactually affect avoidance learning. Avoidance conditioning trials (light followed 5 seconds later by a grid floor shock) began 55 minutes after the injection and the number of crossings was recorded. Three injection conditions were: placebo 0.5 ml peanut oil, weak epinephrine (adrenalin) 0.0125 mg/100 g and strong epinephrine 0.25-0.50 mg/100 g. Rats injected with a weak dose of epinephrine learned a CAR more quickly and effectively than placebo runs, and rats given a heavy dose were significantly poorer learners than the weak epinephrine rats and not significantly better than the placebo rats. The relationship between epinephrine dosage and avoidance learning is nonmonotonic.

Columbia University
New York, N.Y.

2401 Barry, Herbert, III., Miller, Neal E., & Tidd, Gail E. Control for stimulus change while testing effects of amobarbital on conflict. *Journal of Comparative and Physiological Psychology*, 1962, 55, 1071-1074.

Male Sprague-Dawley rats were trained in the Bailey and Miller (1962) telescope alley. After some preliminary training the rats were given 3 days of approach training in the alley, followed by 9 days of approach-avoidance training, using increasing shocks. Food-approach versus avoidance of shock at the goal was tested with hungry rats under 20 mg/kg amobarbital and placebo. Approach performance in the conflict situation was also increased by the shift to a novel condition regardless of whether it was to drug or placebo. This effect of the shift disappeared as soon as shocks were experienced under the novel condition.

Yale University
Hartford, Conn.

2402 Boissier, Jacques R., & Simon, Pierre. La réaction d'exploration chez la Souris (Note préliminaire). [Exploratory reaction in mice. (Preliminary note).] *Thérapie*, 1962, 17, 1225-1232.

A test for the study of psycholeptic drugs is described. The number of holes in a board which are explored by a mouse in a given time under given conditions is recorded. The board is 40 x 40 x 1.8 cm and there are 16 3 cm diameter holes, regularly spaced. The reduction of the number of holes explored after the injection of a drug demonstrates a psycholeptic effect. The parameter for controls in 5 minutes was ca. 41.2. Two drugs (given in mg/kg i.p.) were used to exemplify the technique; with 0.25 chlorpromazine the figure was ca. 35.8, with 0.5 29.4, with 1 21.6 and with 1.5 17.7. With meprobamate, 25 the parameter was ca. 33.2, with 50-32.5, with 100-27.4 and with 150-17.5.

15, rue de l'Ecole de Médecine
Paris, France

2403 Miller, Robert E., & Ogawa, Noruya. The effect of adrenocorticotrophic hormone (ACTH) on avoidance conditioning in the adrenalectomized rat. *Journal of Comparative and Physiological Psychiatry*, 1962, 55, 211-213.

Sixty-seven male Carworth rats were maintained on an ad lib. diet, and after adrenalectomy on 1% saline. Avoidance training was conducted in a 2-compartment apparatus (Murphy and Miller 1955). One week after the adrenalectomy the avoidance-conditioning procedure was begun. One of the 2 randomly selected groups was given 5 mg/kg ACTH i.m., while the other group received a placebo injection. Animals receiving the hormone were significantly slower to extinguish the CAR than were animals which received the placebo. This supports the hypothesis that ACTH has important extra-adrenal effects on behavior.

School of Medicine
University of Pittsburgh
Pittsburgh, Pa.

2404 Fox, Stephen S. Self-maintained sensory input and sensory deprivation in monkeys: a behavioral and neuropharmacological study. *Journal of Comparative and Physiological Psychology*, 1962, 55, 438-444.

Four *Macaca assemensis* and four *M. nemestrina* were used in the investigation of sensory input levels, maintained by the monkey bar-pressing for light rewards. For period of light deprivation a 3 x 3 x 4 foot box was constructed with the addition of a compartment to house 2 mesh-colored 60-watt bulbs. Three experiments were conducted relating to deprivation, adaptation and pharmacology. In Experiment 1, constant and regular rates of response were observed to occur when the response was bar pressing for 0.5 seconds of light. Rate increased with increasing sensory deprivation. In Experiment 2, by partially compensating with light during the test for the need for light produced by deprivation, rates of response were decreased for all deprivation durations. In Experiment 3, injected amphetamine (3 mg/kg) increased

the rate of response for light. It was interpreted that this drug's action indicated an increased requirement of the animal for sensory input. Also the same animals were implanted with deep electrodes and allowed to bar press for light. Recordings taken in the dark and in the response free periods of the response cycle showed regularly increasing percentages of slow activity at very high voltage which appeared immediately preceding a burst of responses. The appearance of these hyper-alpha waves at this time is not due to chance.

University of Michigan
Ann Arbor, Mich.

2405 Aprison, M.H., Wolf, Mary Ann, Poulos, G.L., & Folkerth, T.L. Neurochemical correlates of behavior. III. Variation of serotonin content in several brain areas and peripheral tissues of the pigeon following 5-hydroxytryptophan administration. *Journal of Neurochemistry*, 1962, 9, 575-584.

White Carneaux pigeons were trained in a special multiple unit pigeon elevator (Fenster and Aprison 1960) before being placed in a standard Skinner box. This technique provided a ready source of trained birds for 5HT analysis (4 samples based on function and convenience; telencephalon, cerebellum, pons medulla oblongata and diencephalon plus optic lobes). Assay was made spectrophotofluorometrically. Behavioral techniques were described previously by Aprison and Fersten (1961). The base line used to determine the effects of 50 mg/kg 5HTP i.m. was a multiple 6-ratio 6-interval schedule of reinforcement. Only in the case of the telencephalon and diencephalon (plus optic lobes) did 5HT concentrations pass through a maximum (at 30% of the complete behavior effect-T), and then returned to normal at the same time as behavior returned to normal. 5HT concentrations of the pons medulla oblongata, cerebellum, heart and lung also passed through maxima at the same stage but then returned to normal by 60% of T. Liver 5HT concentrations reached peak values at the same time as did other parts, but did not return to normal during the complete period of study (128% T).

Institute of Psychiatric Research
Indiana University Medical Center
Indianapolis, Ind.

2406 Plotnikoff, N., Reinke, D., & Fitzloff, J. Effects of stimulants on rotarod performance of mice. *Journal of Pharmaceutical Sciences*, 1962, 51, 1007-1008.

After being trained for rotarod performance for 6 minutes, 9 groups of mice received amphetamine (1.25-10.0 mg/kg i.p.), 13 received pheniprazine (2.5-20.0 mg/kg i.p.) and 9 received caffeine (5.0-20.0 mg/kg i.p.). Thirty minutes postinjection rotarod performance was observed for 1 hour to determine drug effects at 3 different rotarod speeds. A dose response relationship was observed with amphetamine. Performance was enhanced in 50% of the animals (ED_{50}) by amphetamine at 2.8 ± 0.4 mg/kg for the A speed, 1.9 ± 0.4 mg/kg for B speed and 5.1 ± 0.5 mg/kg for the C speed. Pheniprazine significantly increased the mean performance time at all 3 speeds, with ED_{50} doses at 6.0 ± 0.8 mg/kg for A, 7.0 ± 1.3 mg/kg for B and 6.5 ± 0.8 mg/kg for C. At C speed, pheniprazine was ineffective in 30 minutes but exerted a pronounced effect in 2 hours. Caffeine produced no significant improvement in performance at any speed.

Stanford Research Institute
Menlo Park, Calif.

2407 Levine, Seymour, & Soliday, Stanley. An effect of adrenal demedullation on the acquisition of a conditioned avoidance response. *Journal of Comparative and Physiological Psychology*, 1962, 55, 214-216.

In order to test theories concerned with anxiety, conditioned fear and avoidance learning which contain the hypothesis that discharge of the sympathetic nervous system is an integral part of fear mediated behavior, male hooded rats were divided into 2 groups, demedullated and non-operated. CAR's were developed in an automatic all-metal Miller-Mowrer type shuttle box. The CS was the sound of a buzzer, 10 seconds followed by the US, a 0.3 ma. shock. The US was terminated when

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the animal left the grid and the CS continued as long as the US was on. Sixty-second intertrial intervals were used. There were no overall significant differences in this system. A 2nd experiment using variations [undisclosed] of the 1st system, i.e., "much more efficient training procedures", showed that demedullates made significantly fewer CAR's than did controls.

Department of Psychiatry
Stanford University
Palo Alto, Calif.

See also 2307, 2363, 2368, 2448, 2498.

2408 Thienes, C.H., Cangelosi, J., & Skilken, R.G. Nicotine and thyroid effects on adrenal catecholamines. Proceedings of the Western Pharmacological Society, 1962, 5, 5-6.

Nicotine (7 mg/kg s.c.) or saline was injected into rats 45 minutes before bilateral adrenalectomy. Biochemical assay of the homogenized adrenals revealed a loss of 55% levarterenol and 30% epinephrine in the nicotine treated groups, with bioassay values of 57% and 26%, respectively. In chronic studies, rats received nicotine injections (0.5-3.75 mg/kg b.i.d.) or saline for 1-4 months. The chronic nicotine groups showed increase in adrenal weight, and epinephrine and levarterenol content, with doubled concentration of the latter. A challenge dose of nicotine (7 mg/kg) in chronic nicotine groups caused some loss of epinephrine and levarterenol, but significantly less than that noticed in acute experiments. This dose of nicotine had no effect on catecholamine concentration in chronic saline groups. Stress accruing from repeated injections may cause catecholamine release masked by compensating increased synthesis. Increase in adrenal weight and catecholamine content suggests an increase in catecholamine storage and synthesis. Studies on thyroid effect on adrenal catecholamines showed a decrease in catecholamine concentration in hyperthyroid and an increase in hypothyroid animals.

Institute of Medical Research
Huntington Memorial Hospital
Pasadena, Calif.

2409 Chatagnon, C., & Chatagnon, P. Recherches sur le rythme d'élimination urinaire, chez l'humain, de chlorpromazine. Considérations biologiques et statistiques. [Studies on the urinary excretory rhythm for chlorpromazine in humans. Biological and statistical considerations.] Annales de Biologie Clinique, 1962, 20, 75-84.

Free and conjugated chlorpromazine in the blood and urine of 3 patients was studied colorimetrically for up to 39 consecutive days. Oral dosage increased from 25 to 900 mg/day then decreased to 0. Highly comparable curves were obtained for the

3 subjects. Excretion stopped when the drug was dropped; there was no accumulation of the compound in the body. Deviations noted in the 3rd case were due to renal pathology.

Laboratoire Central de Biologie
Biologie Nerveuse de Maison-Blanche
Neuilly-sur-Marne, S.-et-O.
France

2410 Palamos Salas, T. Recherches expérimentales et histo-pathologiques sur l'imipramine. [Experimental and histopathologic research on imipramine.] Annales Médico-Psychologiques, 1962, 120, 1, 850.

Chronic and acute experiments with imipramine [dosage unspecified] were made with fish, guinea pigs, pigeons, cats, mice, rabbits and monkeys. Violent imipramine-induced spasms in fish and epileptic crises in monkeys could be reduced with pyridoxine. After chronic treatment diffuse lesions were noted in the brains of animals, with degeneration of Nissl substance and sclerosis. These changes due to chronic intoxication could not be detected by clinical signs. In contrast, 1 monkey died with little evidence of brain lesions following an epileptic seizure in the course of acute experiments with massive doses.

[No address]

2411 Remmer, H., & Siegert, M. Kumulation und Elimination von Phenobarbital. [Accumulation and excretion of phenobarbital.] Archiv für Experimentelle Pathologie und Pharmakologie, 1962, 243, 479-494.

Phenobarbital was administered to dogs (40-100 mg/kg i.v. or 30-61 mg/kg p.o. per day). Plasma levels, determined by UV spectrophotometry, were used to estimate excretion. The rate of excretion is 26.5% per day after a single i.v. dose. After oral administration excretion is delayed for 1-2 days, proceeding afterwards at a similar rate as after i.v. injection. Prolonged administration gradually increases the plasma level to a maximum, and accelerates excretion to a maximum

of 47-61% per day. This high rate was never noted after a single dose. The increased rate of excretion is due to increased oxidation.

Pharmakologisches Institut
der Freien Universität Berlin
Berlin, Germany

2412 Kehl, R., & Czyba, J.C. Sur l'action galactogène de la réserpine chez la lapine. [The galactogenic action of reserpine in rabbits.] *Journal of Physiology*, 1962, 54, 356-357.

Reserpine (0.25-1 mg/day) was injected into 29 juvenile and 66 adult rabbits. Lactation was followed daily. In juveniles, reserpine only caused increased lactation when the rabbits are given concomitant estrogenic treatment. Of the 66 adult females, only 41 showed lactation. Seasonal variation is evident and more positive in the summer; animals under artificial light respond more than those kept in the dark. Some animals which do not respond to reserpine may respond after estrogenic treatment or pinealectomy, but ovariectomized animals do respond. Lactation in normal animals appeared 3-15 days after the beginning of treatment and spontaneously ceased 3 weeks after the cessation of reserpine administration.

Chaire d'Histologie et Embryologie
Faculté de Médecine
Lyon, France

2413 Matthies, H., Decsi, L., & Schmidt, J. Über den Mechanismus der Narkosebeeinflussung durch Iproniazid. [On the mechanism of the effect of iproniazid on narcosis.] *Biochemical Pharmacology*, 1962, 11, 502-504.

Iproniazid (IPN) was injected i.p. (360 μ M per kg) into mice, either 2 or 48 hours before the i.p. (400 μ M/kg) administration of hexobarbital. Duration of anesthesia, and content of hexobarbital and MAO of the entire brain were determined. IPN administered 2 hours before hexobarbital doubled the duration of narcosis; IPN injected 48 hours before hexobarbital re-

duced the duration of sleep about 30%. IPN-treated mice showed higher hexobarbital and lower MAO content than untreated controls, regardless of effect on sleeping time. The narcosis-prolonging effect, but not the shortening effect, is caused by inhibition of hexobarbital breakdown.

Pharmakologische Institut
Medizinische Akademie
Magdeburg, Germany

2414 Frommel, Ed., Vincent, D., Fleury, C., Schmidt-Ginzkey, J. Analgesia, neurovegetative system, cholinesterase and monoaminoxidase. *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 470-475.

Using the dental pulp pain method in guinea pigs, the following sympathomimetics were injected s.c.: epinephrine, levarterenol, oxydrine, ephedrine, amphetamine and dex-amphetamine. A series of parasympathomimetics including acetylcholine were also used, and finally, as blocking agents, cholinesterase and neostigmine. Sympathomimetics, having per se an analgesic effect, are very susceptible to degradation by MAO, therefore the analgesic effect is slight; also these substances exercise an inhibitory action towards MAO, which is highest for amphetamine. Parasympathomimetics having analgesic action fall into 2 classes: those readily inactivated by cholinesterase and those which are resistant. Carbaminoylcholine is resistant and shows the highest analgesic effect, while, logically, acetylcholine is the least active. Nitrocholine, carbaminoylcholine and neostigmine show inhibition of cholinesterase, neostigmine being the most active. Thus the more substance resists enzymic degradation, the more analgesic it is.

Institute of Experimental Therapeutics
Faculty of Medicine
University of Geneva
Geneva, Switzerland

2415 Pflieger, K., Rummel, W., Seifen, E., & Rottman, W. Zur Frage nach der

Ursache des erhöhten Erythrocytenzerfalls unter Phenacetin. [On the causes of the high decomposition rate of erythrocytes under phenacetin administration.] *Medicina Experimentalis*, 1962, 6, 105-112.

Rabbit blood was removed from an ear artery, defibrinated, washed and centrifuged. The centrifuged erythrocytes were then placed in an ice-cold Tyrode solution and tested. Phenacetin, phenetidin, acetanilid and aniline, in concentrations up to 5×10^{-3} m/l had no influence upon the potassium and sodium distribution or on glycolysis in rabbit erythrocytes *in vitro*. Nitrosobenzene (4×10^{-5} m/l) and p-ethoxy-nitrosobenzene (4×10^{-4} m/l) produced a loss of potassium and a gain of sodium and the lactate formation is decreased. The comparison of the methemoglobin produced and the potassium lost in the presence of nitrosobenzene and sodium nitrite makes it evident that no quantitative correlation is present. The measurement of K and Na influx and efflux by means of K^{42} and Na^{22} indicates that nitroso compounds have no influence on active transport but increase passive permeability.

Pharmakologische Institut der Universität
Homburg/Saar, Germany

2416 Kohli, R.P., Sareen, K., Amma, M.K.P., & Gujral, M.L. Anticonvulsant action of indolin-2,3-dione (Isatin). *Indian Journal of Physiology and Pharmacology*, 1962, 6, 145-149.

Rats used to study the anticonvulsant spectrum of indolin-2,3-dione received the following tests: maximalelectroshock seizure threshold (Sareen et al. 1962), minimal electroshock seizure threshold, hyponatremic electroshock seizure threshold, psychomotor seizure threshold, pentetrazol seizures (80 mg/kg s.c.), strychnine (1.5 mg per kg) or picrotoxin (7.5 mg/kg), neurotoxicity studies (Swinyard et al. 1952) and studies on blood pressure and respiration in anesthetized animals. Indolin-2,3-dione manifested anticonvulsant activity in maximal electroshock seizure and hyponatremic electroshock seizure tests in rats with respective ED_{50} 's of 83.7 and 183.3 mg/kg.

It was ineffective in minimal electroshock seizure threshold, psychomotor and pentetrazol tests. High protective indices with lack of side effects warrant further clinical trials.

Department of Pharmacology
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Lucknow, India

2417 Hano, Józef, Giełdanowski, Jerzy, & Kędzierska, Lidia. The action of 5-hydroxypropylbarbituric acids on the central nervous system. *Archivum Immunologiae et Therapiae Experimentalis*, 1962, 10, 353-367.

The chronic action of 5-allyl-5-(β -hydroxy- γ -iodo)-propylbarbituric acid (D_1) and 5-allyl-(β -hydroxypropyl)-barbituric acid (D_1H) on the CNS of mice, rabbits, dogs and humans. The preparations were administered to animals in doses of 0.4-0.5 g/kg during 2-3 weeks. The human experiments were conducted with volunteers who took D_1H as tablets only. Sleeping time after phenobarbital and barbitol was shortened, and, to a smaller degree, after hexobarbital. After chloral hydrate and ether shortening of the time required for narcosis was not observed. Both compounds prolonged sleep, more after phenobarbital and hexobarbital than after the administration of barbitol. The weakest synergistic action occurred after ether and chloral hydrate, preparation D_1 being somewhat more active. D_1 was the stronger antagonist to convulsions induced by pentetrazol, strychnine, picrotoxin and amphetamine. In nontoxic doses it prevented pentetrazol convulsions and strychnine convulsions in 1/3 of the animals; convulsions after amphetamine were delayed and picrotoxin convulsions were unaffected. D_1H only delayed or partially suppressed pentetrazol and picrotoxin convulsions, not affecting strychnine convulsions. It also acted paradoxically by stimulating amphetamine convulsions, both in regard to time of onset and intensity. This is probably due to the ease with which D_1H is converted into allylvalerolactone, which passes into the CSF and 1st paralyzes cortical inhibition, thereby facilitating amphetamine stimulation. In determining the effects of

both compounds on central hypothermia induced by LSD administration, D_1H had hypothermic activity whereas D_1 had no effect. Compulsory motility in mice in a roller cage showed that both compounds inhibited motility. Maze experiments showed a degree of disorientation. Neither compound had any antiemetic effect (against apomorphine i.m. injections in dogs). EEG studies with cortical and hippocampal leads in rabbits showed that D_1H had an effect similar to that of reserpine. Thirty persons were subjected to the Raven test; 20 of them took 100 mg D_1H t.i.d. for 15 days. The test was given before and on the last day of treatment. Mental efficiency was not altered, either in relation to speed or precision. D_1H is considered a tranquilizer.

Department of Pharmacology
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2418 Boissier, J.R., & Pagny, Jeannette. Etude pharmacologique d'une phénothiazine neuroleptique, la thiéthylpérazine ou GS 95 (Torécan). III. Action antivomitique-Discussion générale. [Pharmacological study of a phenothiazine neuroleptic, thiethylperazine or GS 95 (Torecan). III. Antiemetic action-General discussion.] *Medicina Experimentalis*, 1962, 6, 320-326.

Vomiting was induced in dogs by the injection of 100 μ g/kg apomorphine s.c., 15 μ g/kg ergot alkaloids i.v. or 10 mg/kg copper. The antiemetic activity of thiethylperazine was marked at 10 μ g/kg and 300 μ g/kg doses practically suppressed all vomiting. This dose is much lower than that needed for sedation. Its antiemetic activity is slightly greater than that of prochlorperazine and markedly superior to that of chlorpromazine. Apparently there is no necessary relationship between catatonic and antiemetic effects for phenothiazines. Activity-structural substituent in position 3 and the fixed substituents are attached to the extranuclear nitrogen in certain piperazine and sulphur derivatives.

Faculté de Médecine de Paris
Institut de Pharmacologie
Paris, France

2419 Boissier, J.R., Pagny, J., & Evelin, J. Etude pharmacologique d'une phénothiazine neuroleptique, la thiéthylpérazine (Torecan). II. Cction potentialisatrice des hypnotiques. Activité adrénolytique. [Pharmacological study of a neuroleptic phenothiazine derivative, thiethylperazine (Torecan). II. Potentiating action of hypnotics and adrenolytic activity.] *Medicina Experimentalis*, 1962, 6, 136-142.

Various groups of 10 mice received 2.5-20 mg/kg i.p. doses of i.p. or 40 mg/kg hexobarbital i.p. The length of time required to fall asleep and the duration of sleep was measured. Male rats received 25 mg/kg mebubarbital i.p. or 250 mg/kg chloral hydrate. Upon awakening, animals received thiethylperazine, 5-10 mg/kg i.p. In both experiments animals fell asleep quickly (1-7 minutes for mice and 0-10 minutes for rats). Duration of sleep varied from 5 minutes to more than 1 hour. Thiethylperazine injections resulted in a decline in temperature during the first half hour of 1-1.6°, which returned to normal within 1-3 hours. Guinea pig seminal vesicles were placed in a buffer solution at 39°, and epinephrine at concentrations of 1×10^{-8} M to 4×10^{-8} M was added. At a concentration of 5×10^{-8} M, thiethylperazine decreased epinephrine contraction by 50%. When injected i.v. into rabbits at doses of 0.2-0.5 mg/kg thiethylperazine will either decrease or suppress hypertension due to epinephrine. At doses of 0.5-1.0 mg/kg it will reverse this hypertensive effect. Results of similar experiments with dogs were not as conclusive.

Faculté de Médecine
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2420 Ríos, Oscar. Aspectos preliminares al estudio farmacopsiquiátrico del ayahuasca y su principio activo. [Preliminary aspects in the pharmacopsychiatric study of ayahuasca and its active principles.] *Anales de la Facultad de Medicina (Lima)*, 1962, 45, 22-66.

The South American plant *Cabi paraensis* (ayahuasca) and its active principle harmine are detailed. Identification of harmine was made spectrophotometrically. Marin's

952) method of extraction for alkaloids was used. Pharmacodynamic studies were conducted with dogs and cats, proving typical harmine effects.

Facultad de Medicina
Universidad Nacional Mayor de San Marcos
Lima, Peru

2421 Scherrer-Etienne, M., Giacomelli, G., Rüphi, M., & Posternak, J.M. Etude de la répartition de l'éthanol dans le cerveau du chat par autoradiographie. [Study of the distribution of ethanol in the brain of the cat by autoradiography.] *Journal de Physiologie*, 1962, 54, 412-413.

Ethanol was injected i.v. into cats as a 50% solution in doses of 80-300 mg/100 g, containing 10 μ c ethanol C 14-1. Animals were sacrificed 1-80 minutes after injection. Four mm slices of the head were cut in the frontal plane (-70°C). One minute after the beginning of injection the distribution of ethanol in the brain appears to depend on localized blood flow. Structures with high blood supply are most enriched in ethanol, the lowest concentration being in the white matter. Five minutes later concentrations tend to equalize in the gray substance. Up to 30 minutes after injection, particularly high activity is observed at the level of the cerebral ventricles; after an hour this drops. Gray matter then shows homogeneous distribution, but remains more active than white substance. The appearance of an eventual metabolite of ethanol, acetate has been autoradiographically noted. Control experiments in cats with C 14-1-acetate shows that its effect is negligible. The penetration of acetate into cerebral tissue is slower than that of ethanol. Moreover an equivalent injection of acetate gives a very weak autoradiograph image compared to that of ethanol.

Institut de Physiologie
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Geneva, Switzerland

2422 Gordon, Malcolm W., Sims, James A., Hanson, Rolf K., & Kuttner, Robert E. The effects of some psychopharmacological agents and other drugs on the uptake of an amino acid by brain. *Journal of Neuro-*

chemistry, 1962, 9, 477-486.

Fasted female rats injected i.p. with 1 ml saline containing [1-C¹⁴] α -aminoisobutyric acid (AIBA) were studied. Specific activities ranged from 8-16 μ c/mg. Animals were decapitated after 40 minutes or 4 hours and tissues examined via digestion and CO₂ liberation in scintillometer. Drugs were injected i.p. either before or simultaneously with the radioactive amino acid. Substances used were trypsin, trypan red, β -lactoglobulin, starch, physostigmine, acetazolamide, pentetrazole, mescaline, iproniazid, reserpine, chlorpromazine, levarterenol and 5HT. Some of these were included because of reported influence on the blood-brain barrier. Many agents were found effective in depressing AIBA uptake in short-term experiments (40 minutes), but even repeated injections of active drugs were found ineffective in 4 hour experiments. The possible involvement of the neurohormones in brain transport is also discussed.

Biochemical Research
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2423 Biljani, J.C., Gulati, O.D., Gokhale, S.D., & Joseph, A.D. An investigation of the antiepileptic action of treburon. *Indian Journal of Physiology and Pharmacology*, 1962, 6, 129-136.

In a series of tests in which 3 different doses of treburon were tested against a fixed dose of the agonist (preliminarily determined as the amount which would produce 100% anesthesia in almost all animals). Groups of pigeons and rats were used. In most trials groups of 10 animals were used, pigeons i.v. injected and rats i.p. injected. Agonists were: thiopental (20 mg/kg), pentobarbital (30 mg/kg), phenobarbital (100 mg/kg). The results of a large treburon dose (120 mg/kg) was also studied as well as the possible antidepressant action of helparin and picrotoxin. Thiopental, pentobarbital and phenobarbital were antagonized respectively by treburin at: 30 and 45 mg/kg; 30, 60 and 90 mg/kg, and 60, 90 and 120 mg/kg. For paraldehyde, treburin (30, 60 and 90 mg/kg) did not significantly reduce

the duration of anesthesia. Heparin (10 mg./kg) did not antagonize these drugs while picrotoxin (0.05 mg/kg) antagonized phenobarbital. The antibarbiturate effect of treburin was dose related, best against thio-pental and least against phenobarbital. The lack of effectiveness against paraldehyde indicates that treburin may have a specific antibarbiturate effect, possibly mediated through competition for a common site in the CNS. Further tests, however, are necessary to confirm this. High doses of treburin had no convulsive action and in view of the hazards of currently available analeptic agents, further study of treburin is indicated.

Department of Pharmacology
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Baroda, India

2424 Viljanto, J., Isomäki, H., & Kulonen, E. Effect of aminoacetonitrile, iproniazid and semicarbazide on the tensile strength of experimental granulation tissue. *Acta Pharmacologica et Toxicologica*, 1962, 19, 191-198.

Implantation and measurement of tensile strength as described by Viljanto and Kulonen (1962) was made in 421 Wistar rats fed test substances 7 days following implantation. Both aminoacetonitrile (25, 50 or 100 mg/100 g) and semicarbazide (25 mg/100 g) decreased tensile strength in developing granulation tissue. A similar but probably less specific effect was observed following administration of iproniazid (2, 5 or 10/100 g). The weight and nutritional state of the animal were important factors in the production of tensile strength. While normally tensile strength developed slowly in aminoacetonitrile-treated animals but hydroxyproline production was not inhibited to the same degree. The total nitrogen in the granulation tissue rose most rapidly in the controls before collagen synthesis. In aminoacetonitrile treated animals the nitrogen content of the granulation tissue persisted at the 5th day level.

Department of Medical Chemistry
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2425 Soulairac, A., & Soulairac, M.L. Effets de l'administration chronique de reserpine sur la fonction génitale du rat mâle. Modifications du comportement sexuel, du tractus génital et altérations du système nerveux central. [The effects of chronic reserpine administration on the genital function of the male rat; modifications in sexual behavior, the genital tract and alterations in the central nervous system.] *Annales Endocrinologie*, 1962, 23, 281-292.

The sexual behavior of male rats was studied after reserpine administration: 25 µg/100 g/day for 15 days, and 60 µg per 100 g per day for 4 days. At the low dosage reserpine markedly increased the number of ejaculations and significantly decreased the number of intromissions preceding each ejaculation. At high dosage the drug modified sexual behavior in a similar manner at the 2nd day but 2 days later the animals were in a stuporous state and all tests were negative; 5 days after cessation of treatment normal sexual behavior returned. The testes deteriorate at the interstitial level with fibrocytic involution and the efferent canal shows marked reduction in the columnar height of its epithelium. In the CNS, neuronal deterioration is particularly clear in the lateral mammillary nuclei of the hypothalamus. This localized neurotoxic action of reserpine provides one possible explanation for the effect of this compound on male genital functions.

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2426 Otsuka, Yasuo, Sakai, Fuminori, Sakuma, Akira, Saji, Yoshiaki, Nakanishi, Suehiro, & Sawabe, Takashi. Central effects of phencyclidine hydrochloride (Sernyl). *Japanese Journal of Pharmacology*, 1962, 12, 104-110.

Phencyclidine's central action was studied in cats. Immediately after 1-2 mg/kg i.v., the animals lost the righting reflex, respiration became irregular and in-

spiratory spasticity prominent. Nystagmus and mydriasis, knee jerk reflex exaggeration and the presence of the tonic neck reflex were noted. Three to 12 hours after injection heavy ataxia with a peculiar shaking of the head was noted. The anesthetic dose was estimated to be 1.7 mg/kg. In curarized cats, cortical and subcortical EEG activity, multiple spikes and/or fast wave bursts were alternately superimposed on the background with marked changes in the suprasylvian gyrus and hippocampus. Phrenic volleys were depressed and markedly prolonged. Blood pressure was slightly elevated following an initial drop. When a 1% solution of phencyclidine was topically applied to the cortical surface near the electrodes, high-voltage waves were periodically reported, most frequently observed in the anterior sigmoid gyrus. The periodicity of these waves was closely related to that of a phrenic volley. Patterns were considerably modified by transection of the brain stem at various levels.

Department of Pharmacology
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Tokyo, Japan

2427 Arvay, A., Nyiri, I., Rakosi, M., & Buris, L. Contribution à l'étude des modifications du fonctionnement de l'adenohypophyse par des substances pharmacologiques. [Effect of certain pharmacological substances on changes in the functioning of the adenohypophysis.] *Annales d'Endocrinologie*, 1962, 23, 186-199.

Female rats received p-oxy-acetophenone (POA), p-oxy-propiofenone (POP), o-oxy-propiofenone (OOP), p-oxy-butyrophenone (POB), o-oxy-chalcone, resacetophenone, chlorpromazine and phenobarbital, 20-40 mg per day, chlorpromazine p.o. and all others injected. o-Oxy-chalcone, resacetophenone and POB increase the duration of estrus, and with administration of POB, most animals were in a state of permanent estrus. OOP, POP and POA increased the intervals between estrus cycles and

frequently caused a state of permanent diestrus. After 3-4 weeks the animals were decapitated. POB increases while POA and POP decrease the percentage of Schiff-positive cells, which indicates production and inhibition of gonadotropin respectively. The drugs generally induced thyroid hyperfunction; POB, POP and POA immediately, and chlorpromazine after a brief period of hypofunction. POB causes endometrial hyperproliferation and the intensification of Graafian follicle maturation. POA inhibits maturation. Reduction in levels of endogenous estrogenic compounds following POA, POP, chlorpromazine and phenobarbital administration is accompanied by increased production of thyrotropic hormone, luteinizing hormone and luteotropic hormone.

Institute of Organic Chemistry
Debrecen, Hungary

2428 Romanowski, W., & Monnier, M. Influence de GABA et du thiosemicarbazide (TSC) sur l'activité électrique du cerveau du lapin. [Influence of GABA and of thiosemicarbazide (TSC) on the electrical activity in the rabbit brain.] *Acta Physiologica Polonica*, 1962, 13, 399-406.

Seven rabbits received i.v. injections of 6-20 mg/kg thiosemicarbazide (TSC). Tremors of the paws and clonic and tonic convulsions were noted at the lower doses, death intervening at doses of 14-20 mg/kg. GABA injection had no effect on TSC-induced symptoms. Heart action was slowed down during the 1st 10 minutes and again after 2 hours. Large 2-3 cps delta waves appear in the cortex, the number of spindles increases—the hippocampus is activated. Convulsions were preceded by abnormal synchronization of the activity of the hippocampus, caudate nucleus and the median thalamus. Administration of GABA (2 mg/kg i.v.) resulted in the replacement of the TSC tracing by an arousal pattern with desynchronization of the neocortex and synchronization of the archicortex and subcortex. High frequency stimulation of the mesenceph-

alic reticulum also induces similar reactions. Stimulation of the median thalamus under TSC increases the cortical recruiting potentials. The substance also increases the cortical potentials of hippocampal origin and the excitability of the hippocampus.

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Basel, Switzerland

2429 Fleming, William W. Supersensitivity of the cat heart to catecholamine-induced arrhythmias following reserpine pretreatment. *Proceedings of the Society of Experimental Biology and Medicine*, 1962, 111, 484-486.

Reserpine (0.1 mg/kg/day i.p.) was administered to 26 cats for 7-28 days to produce maximal depletion of heart levarterenol. Cats were then pithed under ether anesthesia, after which they received consecutive single injections of levarterenol or epinephrine (0.01-100 µg/kg i.v.) until cardiac arrhythmias were observed. Ventricular premature systoles and extrasystoles constituted the initial arrhythmias, followed in some instances by ventricular tachycardia or fibrillation. Threshold doses (appearance of 1st cardiac arrhythmia) were established for reserpine. Statistical significance of sensitivity change was determined by Chi-square analysis. Reserpine treated animals showed significantly greater sensitivity to levarterenol and epinephrine than did controls. Dose-response curves for positive chronotropic and pressor effect were shifted slightly to the left, indicating supersensitivity after the 7, 14, 21 and 28 day reserpine treatments. Sensitivity to levarterenol and epinephrine induced arrhythmias becomes progressively greater with increasing length of reserpine treatment.

Department of Pharmacology
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2430 Faure, J. La phase "paradoxale" du sommeil chez le Lapin (ses relations neurohormonales). [The "paradoxical" phase of sleep in the rabbit (its neuro-

hormonal relationships).] *Revue Neurologique*, 1962, 2, 190-196.

EEG's and electromyograms (EMG's) were recorded for 15 rabbits and their movements under different stimuli observed the animals being kept in a soundproof lighted room. Spontaneous occurrence of the "paradoxical sleep" (i.e., an EEG corresponding to the awakening stage, with an EMG showing complete loss of muscle tonus) was noted in about 1/2 the rabbits over a 2-month period. Partial paradoxical sleep, i.e., some tonus persisting despite considerable relaxation of the muscles was noted in all rabbits. Neurohypophyseal hormones, e.g., Vasopressine Lysine at doses of 500 mUI/5 kg induces the complete state in 90% of the cases. Electrical stimulation of the median and paramedian dorso-tegmento-mesencephalic and oropontic regions also provokes this paradoxical phase.

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2431 Higuchi, Hideo. Effects of intravenous and intracarotid administration of reserpine on catecholamine contents of the brain, heart and adrenal gland in rabbit. *Japanese Journal of Pharmacology*, 1962, 12, 34-47.

The effects of reserpine on catecholamine content in brain, heart and adrenal gland tissue was studied in rabbits in conjunction with behavioral effects. Administration of 1.0 mg/kg reserpine i.v. decreased the brain and peripheral catecholamine content and the course of amine depletion coincided with the characteristic sedation induced by reserpine. The tissue amine content was also considerably depleted by i.v. injection of 0.1 mg/kg reserpine. Amine reduction, however, was considerably less than that with 1.0 mg/kg reserpine. Amine depletion in the atria by 0.1 mg/kg reserpine was almost the same as that induced by 1.0 mg/kg. Intracarotid injection of 0.1 mg/kg reserpine slightly increased or failed to modify amine content in whole brain and brain stem within the 1st 1/

four of administration. At this time, rabbits showed slight central excitement. Hereafter, decreased amine content almost resembled that produced by i.v. injection reserpine. Intracarotid injection of 0.0 mg/kg reserpine more markedly depleted the amine content of brain and peripheral organs than did the decrease in amine level produced by i.v. administration of the same dose. The 10% decrease in atrial levarterenol and adrenal epinephrine within the 1st 1/2 hour of administration suggests the accumulation of levarterenol in the central sites did not precipitate a decrease in levarterenol content in innervated peripheral organs like the heart and adrenal glands.

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2432 Spector, Sydney, Melmon, Kenneth, Sjoerdsma, Albert. Evidence for rapid turnover of norepinephrine in rat heart and brain. *Proceedings of the Society of Experimental Biology and Medicine*, 1962, 111, 79-81.

Male Sprague-Dawley rats and controls received single injections of Win 18501-2 (60 mg/kg i.p.) after which animals were sacrificed and tissues analyzed for serotonin and levarterenol by the method of Bogdanski et al. (1956). Some animals also received pretreatment with i.p. N-methyl-1-benzyl-propargylamine (MO-911, 75 mg per day) or bretylium tosylate (20 mg/kg) to elucidate the mechanism by which Win 18501-2 produced levarterenol depletion. Levarterenol heart content declined profoundly with Win 18501-2 in 3 hours, but levels returned to 50% of normal in 6 hours and attained normal values (80-90% of control levels) in 8 hours. Brain levarterenol content declined by 60% in 3 hours. Serotonin levels were unaltered in brain tissue. Win 18501-2 produced definitive, persistent CNS depression within 5 minutes. Pretreatment with MO-911 prevented the decline in brain and heart levarterenol concentrations. The Win 18501-2 induced depression was not reversed by pretreatment with MO-911. Similarly, bretylium

failed to prevent release of heart levarterenol.

Experimental Therapeutics Branch
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2433 Boissier, Jacques R. *Pharmacologie des anorexigènes*. [Pharmacology of anorexigenics.] *Thérapie*, 1962, 17, 803-825.

Four dogs were trained to eat 1 meal per day within a 30-minute period. After 2 weeks of training, the dogs received 1 mg/kg amphetamine 1 hour before feeding time. After 30 minutes, the remaining food was weighed. Amphetamine administration was stopped, and the dogs continued on the same diet for another 2 weeks. Modifications of this experiment in which dogs were allowed to feed at will but were given amphetamine at stated intervals during the day were also conducted, as were experiments on rats subjected to a similar regimen. These results, and some obtained with rats indicate that amphetamine is truly anorexigenic, and that its action is greater in adults than in the young. Tachyphylaxis occurs after a certain period. When medication is stopped and resumed at a later time, the anorexic effect recurs. In the treatment of obesity with the wide range of amphetaminelike agents available, these compounds act as a sort of psychotherapy they are psychoanaleptic adjuncts to conventional management, i.e., diet restriction, etc.

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Paris 6, France

2434 Ernst, A.M. Experiments with an O-methylated product of dopamine on cats. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 48-53.

To test the supposition that the hypokinetic rigid syndrome could be suppressed by administration of phenylethylamine or by DOPA, 20 cats were injected with bulbo-capnine 15 mg/kg and 20 cats administered papaverine 35 mg/kg. When catatonia was fully established (20 minutes after the 1st

injection) 6 animals of each group were used as controls and 7 animals were injected with either 80-100 mg/kg phenylethylamine or 100 mg/kg DOPA. Papaverine treated cats gained full motility after 30 minutes and controls remained catatonic about 1 additional hour. The bulbocapnine treated animals did regain the free motility of their heads 10 minutes after phenylethylamine or DOPA and were able to look behind but could not move either forelegs or hindlegs. Their catalepsy disappeared almost at the same time as the catatonia of the controls. As well, 2 groups of 20 cats each were injected with 60 mg/kg 3,4-dimethoxy-phenylethylamine and 50 mg per kg mescaline respectively. Six control animals of each group were catatonic for 1.5 to 2.5 hours while 7 animals of each group administered 100 mg/kg phenylethylamine and 7 animals injected with DOPA regained motility within 30 minutes. As the O-methylated products could easily pass the blood-brain barrier, contrary to dopamine itself, the disturbance in dopamine metabolism does not necessarily take place exclusively in the brain but may, for instance, also originate in the liver. Further, in human patients phenomena of the hypokinetic rigid type may be caused by O-methylation of dopamine in the para position as supported by the antagonistic effects of phenylethylamine and of DOPA on cats pretreated with O-methylated products of dopamine.

[No address]

2435 Mercier, J., & Dessaigne, S. Etude psychopharmacologique et neurophysiologique d'un dépresseur médulaire, myorésolutif: le 2-(4-chlorophenyl)-3-méthyl-4-méthathiazanone-1-dioxyde (Win 4692-Trancopal). [Psychopharmacological and neurophysiological study of a muscle relaxant and medullary depressor: chlormezanone (Win 4692 - Trancopal.) Anesthesia Analgesia, 1962, 19, 603-626.

The LD₅₀ for chlormezanone was determined in mice as 514 mg/kg i.p. The hypnotic dose is 250 mg/kg in mice, and 175 mg/kg in rats. Motor activity is slightly affected in mice at 100 mg/kg and in cats at 200 mg/kg. The drug decreases motor

activity and exercises a sedative effect at doses which do not depress reflexes or encephalic centers. The ratio between the initial effective dose and the LD₅₀ is 1:17. Except at doses of 200 mg/kg, when 40% of the test animals died, the drug does not reduce psychomotor agitation produced by amphetamine, but does retard the onset and shorten the duration. At doses of 120 mg/kg it will suppress psychomotor hyperactivity induced by 20 mg/kg s.c. morphine in 50% of the cases; at 150 mg/kg the effects are fully suppressed. At 30 mg/kg administered 30 minutes before s.c. injection of 85 mg/kg pentetrazol (100% convulsive and 75% lethal dose), the pentetrazol convulsions were suppressed in 50% of the cases. Suppression was total at 50 mg/kg. Intraperitoneal administration of 50 mg/kg provided 100% protection against electric shock and 40 mg/kg provided 50% protection against shock administered 30 minutes later. Chlormezanone provided poor protection against the central-convulsant effects of strychnine but effectively antagonizes the lethal effects of this alkaloid. At 25 mg/kg i.v. it depresses and considerably prolongs the polysynaptic reflexes in spinal cats. EEG's of cats and rabbits under reticular cortical, mono- and polysynaptic reflex excitation, indicate that the properties of chlormezanone are due to depression of medullary neurons.

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2436 Buchel, L., & Levy, J. III.- Action du triperidol au niveau du système nerveux autonome. [Action of triperidol at the level of the autonomic nervous system.] Therapie 1962, 17, 1085-1094.

Triperidol was injected i.v. (17-1000 µg/kg) and i.m. into male Wistar rats. Its vascular action is highly variable, hypotension appearing at 33-1000 µg/kg i.v., and 31-3 µg/kg i.m., but only transiently. It has pronounced adrenolytic action, especially when administered i.m. at the above state dose. It is also antagonistic to serotonin hypertension at doses of 34-72 µg/kg. It is not antagonistic to acetylcholine at 32-8

re to reduce hypertension at 1000 $\mu\text{g/kg}$, but neither triperidol nor haloperidol affect histamine hypotension except at very high doses (44 and 1750 $\mu\text{g/kg}$ respectively). Similar results were registered on rabbits with respect to vascular and adrenolytic action. At doses of $12.5\text{--}25 \times 10^{-7}$ triperidol begins to lower the tonus of isolated rat duodenum. At concentrations about 10 times as great, it has a weak and variable, reversible spasmolytic atropinic effect. Its papavernic spasmolytic effect is approximately double that of adiphenine and lasts even after 60 minutes. Both tri- and haloperidol have a strongly adrenolytic effect in vitro. It has antihistaminic properties at concentrations of the order of 10^{-7} on the isolated guinea pig ileum. Its anticholinergic action is very feeble.

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2437 Mustala, O.O., & Penttilä, O.I. Anticonvulsant action of some new skeletal muscle relaxants on strychnine convulsions in mice. *Acta Pharmacologica et Toxicologica*, 1962, 19, 247-250.

The anticonvulsant effect of phenobarbital, chlordiazepoxide, chlormezanone, chloroxazone, mephensin, methocarbamol and mepyramidol were investigated against strychnine convulsions in mice. The LD_{50} , PD_{50} and the dose preventing death (DPD_{50}) were established for each of these values in 5-60 test animals at 24° . Only chlordiazepoxide and chlormezanone were superior to phenobarbital in preventing death induced by strychnine. In preventing convulsions, phenobarbital was about as effective as chloroxazone, mephensin, and methocarbamol. Chlordiazepoxide and chlormezanone were superior to the other substances tested. Chlordiazepoxide had the highest $\text{LD}_{50}/\text{DPD}_{50}$ and chlormezanone the highest $\text{LD}_{50}/\text{CPD}_{50}$. Mepyramidol could not prevent convulsions at any dose level. The activity of the other substances investigated was similar.

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Helsinki, Finland

2438 Titus, E.O., & Spiegel, H.E. Effect of desmethylimipramine (DMI) on uptake of norepinephrine- 7H^3 (NE) in heart. *Federation Proceedings*, 1962, 22, 179.

Cat heart slices which normally take up levarterenol- 7H^3 to levels which are 3-5 times those obtained in buffer do not concentrate the labeled levarterenol when 10^{-6} M desmethylimipramine (DMI) is added with partial inhibition at 10^{-10} M. Radioactive levarterenol in mouse heart 1 hour after i.v. administration of 10 $\mu\text{g/kg}$ is 15.1 $\text{m}\mu\text{g}$ in controls and 4.5 $\text{m}\mu\text{g}$ in animals receiving 10 mg/kg DMI 1 hour before levarterenol. DMI appears to compete with levarterenol for sites of uptake, since a 250% increase in levarterenol dosage results in normal DMI uptake in mice. DMI does not deplete levarterenol. Reserpine (0.1 mg/kg) administered 1 hour after levarterenol depletes heart radioactivity to 19% of controls. The competitive relationship between the levarterenol and levarterenol inhibitors may govern the capacity of these drugs to deplete levarterenol.

National Institutes of Health
Bethesda, Md.

2439 Eechaute, W., Lacroix, E., Leusen, I., & Bouckaert, J.J. L'Activité du cortex surrénalien sous l'influence de la reserpine et de l'iproniazide. [The activity of the adrenal cortex under the influence of reserpine and iproniazide.] *Archives Internationales de Pharmacodynamie et de Thérapie*, 1962, 139, 403-414.

Male rats were separated into 5 groups. Two groups received 5 mg/kg reserpine, 1 group received 3 mg/kg , controls in these groups receiving 0.5 ml saline, all i.p. These 3 groups, who had received the "acute treatment" were killed 3, 9 and 20 hours after administration of the single dose. One group received 2.5 mg/kg reserpine for 4 days and the 5th group 1 mg/kg for 10 days. These were sacrificed 4 hours after the final reserpine injection. Some animals received single doses of 100 mg/kg iproniazide i.p. 6 hours before reserpine administration. Both acute and chronic treatments produced a marked

and prolonged increase of plasma corticosterone levels and of the steroid production by the adrenals in vitro. Pretreatment with iproniazide prevented, in both acute and chronic conditions, the adrenocortical response to reserpine. On the other hand, reserpine did not appear to block adrenocortical response to acute cold stress (4°C for 60 minutes).

Laboratoires de Physiologie
Université de Gand
Gand, Belgium

2440 Luštinec, K. The effect of some drugs on oxygen consumption in rats under basal conditions and during cold stress. *Physiologia Bohemoslovenica*, 1962, 11, 343-350.

The effects of the following drugs (mg/kg i.p.) on basal oxygen consumption was studied in rats: phenobarbital (150), pentobarbital (15, 30 and 45), urethane (1.5-2), mephensin (40 and 80), pentamethonium (90), chlorpromazine (20), promethazine (20), reserpine (5), and yohimbine (20); the following were used s.c.: chloralhydrate (600 mg/kg), dihydroergotoxin (0.4), quinine (130) and amidopyridine (140). Oxygen consumption was measured by a modification of the Regnault-Reiset system of indirect calorimetry. Artificial respiration was maintained during the use of narcotics. For cold stress the metabolimeter was immersed in a mixture of ice and water. Here nearly all substances had a depressive effect which was usually the same, if not greater than that for classic artificial-hibernation producing substances such as chlorpromazine. The effect of reserpine is slight even though high doses were used; that of dihydroergotoxin which is used in lytic cocktails instead of chlorpromazine is doubtful. Synergism between hibernation producing substances is evident during cold stress, whereas it is not present at ambient temperatures. At 26°C, none of these drugs decreased basal metabolism if this is defined as oxygen consumption during sleep. These drugs act nonspecifically and do not affect biological oxidation.

Institute of Industrial Hygiene and
Occupational Diseases
Prague, Czechoslovakia

2441 Imamura, Goro, & Kawamura, Hiroshi. Activation pattern in lower level in the neo-, paleo-, and archicortices. *Japanese Journal of Physiology*, 1962, 12, 495-505.

In ether-anesthetized cats with tracheal and venal canulas inserted, needle electrodes were stereotaxically placed in the amygdala, hippocampus, midbrain reticular formation, preoptic region and posterior hypothalamus, as well as some other subcortical nuclei. Square-wave pulses for stimulation were delivered from an electronic stimulator and EEG's made on a 12-channel machine. After the animal was fixed on the stereotaxic apparatus, ether was stopped and d-turbocurarine was injected; respiration was maintained artificially. High amplitude 10-15 cps (even 4-20 cps) rhythmic waves, termed "activation pattern in the lower level" in the neo-, paleo- and archicortices, were then studied. This activation pattern was invoked by depressants: pentobarbital (8-10 mg/kg i.v.), hexobarbital (5 mg/kg i.v.), meprobamate (1 g/kg i.p.) and chlorpromazine (30 mg/kg i.v.). Meprobamate or a small dose of barbiturate produced the lower level activation pattern in the neocortex. In recovery from deep anesthesia this pattern is often observed in the amygdala, pyriform lobe, then hippocampus and lastly in the neocortex. The same pattern in all areas was obtained by 10 mg caffeine i.v. 4 hours after meprobamate administration. Without depressants, stimulation induced the activation pattern in the hippocampus more easily than in the neo- and paleocortices. The pattern was also observed in the paleocortex and amygdala following a large dose of chlorpromazine. Five classes of EEG patterns in the cortices were established which corresponded to behavioral activity levels.

Department of Psychology
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Tokyo, Japan

2442 Frommel, E., Fleury, C., von Ledebur, I., & Béguin, M. D'un antidote partielle de la chlorpromazine: la fièvre vaccinale. Discussion pharmacodynamique. [A partial antidote to chlorpromazine: vaccinal fever]

pharmacodynamic discussion.] *Thérapie*, 1962, 17, 1333-1347.

Time-temperature curves were obtained for mice, guinea pigs, and rabbits, under administration of various drugs. Simultaneous injection of Pyrexal (lipopolysaccharide preparation of *Salmonella equi*) and chlorpromazine shows that the former is antagonistic to the hypothermic effects of the latter. Pyrexal administration prolongs the duration of sleep due to phenobarbital, decreases that due to chlorpromazine, and shortens the duration of sleep due to phenobarbital-chlorpromazine association. Both chlorpromazine and Pyrexal prolong hexobarbital-induced sleep, and Pyrexal slightly increases duration of sleep due to hexobarbital-chlorpromazine association. Similar effects were recorded with respect to thiopental. Pyrexal shortens sleep due to morphine, and that due to morphine-chlorpromazine association, but without correcting the hypothermia in the latter case. The same results were noted for chlordiazepoxide alone and in association with chlorpromazine. Pyrexal diminishes the analgesic property of morphine and of morphine-chlorpromazine, and has no effect on chlorpromazine-induced electrocrises. Both chlorpromazine alone and chlorpromazine-Pyrexal inhibit psychomotor agitation induced by amphetamine. Pyrexal reduces the anticontractile anticholinergic properties of atropine and opiates and also potentiates the antihistaminic activity of promethazine.

Faculté de Médecine
Geneva, Switzerland

2443 Bernhard, Karl, & Beer, Hermann. Aktivitäten der Expirationskohlendioxid, des ZNS und anderer Organe nach Gaben von ^{14}C -signiertem N-(α -Dimethyl-amino-propyl)-iminodibenzyl (Psychopharmakon Profril) an Ratten und Hunde. [Activity of exhaled carbon dioxide, the CNS and other organs in rats and dogs after administration of ^{14}C -labeled imipramine.] *Helvetica Physiologica Acta*, 1962, 20, 114-115.

The rate of systemic dissemination of imipramine (10 mg in saline through a

tracheal tube) was studied in rats. Animals were killed 15, 30 and 60 minutes after drug administration. Similar experiments were performed on dogs with 25 mg imipramine i.p. The dogs were sacrificed after 30 minutes, 2, 4 or 24 hours. Total activity of exhaled carbon dioxide in rats over a 24-hour period varied between 26 and 42% with an average of about 34%. Short-term activity amounted to less than 0.5% after 15 minutes, and about 5% after 1 hour. Total and specific activities were measured in different parts of the brain, liver, kidneys, gall bladder, blood, urine, musculature and various adipose tissues. More than half the imipramine is absorbed within 15 minutes after oral administration, followed by rapid demethylation. Imipramine may be detected in an unchanged or partially (1-2%) changed form in the CNS. Specific activity was highest in the cerebrum.

Physiologische-Chemische Institut
Universität Basel
Basel, Switzerland

2444 Murphy, M. Lois. Teratogenic effects in rats of growth inhibiting chemicals, including studies on thalidomide. *Clinical Proceedings, Children's Hospital of the District of Columbia*, 1962, 18, 307-322.

Thalidomide (2 g/kg i.p. in 1 or 2 doses) was administered on day 12, or days 11 and 12, or 12 and 12, to 16 pregnant rats. Abnormalities resulted in 2 litters, complete resorption in 1, more than 50% resorption in 3 and normal litters in 10. Various cancer chemotherapeutic agents (alkylating agents and antimetabolites) were also administered i.p. in 1 or more doses of 0.05- greater than 2500 mg/kg/day to pregnant rats on days 9, 10, 11, 12 or 17 of gestation. Results indicated that 1 injection administered from day 9 to day 14 resulted in malformed appendages, brains, palates, lips, viscera, tails and bones. Comparative dosages are proffered in tabular form for LD₅₀'s in adult rats, minimal LD₁₀₀'s in fetuses, teratogenic doses and maximal doses which gave neither resorption nor teratogenic effects in fetuses. In contrast to statistics obtained with thalidomide, cancer-inhibiting drugs produce abnormalities at teratogenic dosages in over 90%

of embryos.

Division of Experimental Chemotherapy
Sloan-Kettering Institute for Cancer
Research
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2445 Lecomte, J., & Troquet, J. Antagonisme entre salicylate de soude et bradykinine chez le rat. [Antagonism between sodium salicylate and bradykinin in the rat.] *Archives Internationales de Physiologie et de Biochimie*, 1962, 70, 735-737.

In anesthetized rats, 1 of the common carotid arteries was separated without vagotomy and blood pressure recorded manometrically. All substances were injected i.v., usually in divided doses. Seventeen agents, including promethazine, BOL and phenylbutazone, were tested against 0.5-2.0 μ g/100 g bradykinin. All substances except sodium salicylate (25-50 mg/100 g) had no effect. Sodium salicylate almost completely countered the marked drop in blood pressure caused by bradykinin.

Institut Léon Fredericq
Université de Liège
Liège, Belgium

2446 Charpentier, Jean. Analyse de l'action analgésique de la morphine chez le rat par une nouvelle méthode quantitative. [Analysis of the analgesic action of morphine in the rat by new quantitative methods.] *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences*, 1962, 255, 2285-2287.

Morphine was injected i.p. into male rats at 4, 8 and 16 mg/kg. Twenty to 50 minutes after injection the reaction threshold to electric tail shock, as a function of voltage (0-150 volts), and increased the central excitability after a 75 volt shock were assayed. Central excitability decreased as follows (mg/kg): 4-16%, 8-51% and 16-29%; the latter result seems to be due to the fact that the excitability of the animal is already much diminished by the 1st shock.

Laboratoire de Psychophysiologie
Faculté des Sciences
Paris, France

2447 Carraz, G., Boucherle, A., Beriel S.H., & Duc, Luu. Action de quelques amines du groupe de la phénothiazine et de certains de leurs dérivés chloréthylés sur le sarcome d'Ehrlich de la Souris. I. Action sur la consommation cellulaire d'oxygène. [The action of some phenothiazines and certain of their chlorethyl derivatives on Ehrlich's sarcoma in mice. I. Influence on cellular oxygen consumption.] *Thérapie* 1962, 17, 8-18.

Ascites cells from Swiss mice were used in manometry (oxygen consumption) with a number of phenothiazine compounds at 2 concentrations. Phenothiazines of the chlorpromazine type increased oxygen consumption slightly at small doses, but high doses with lower consumption. Compound with an aliphatic chain on the nitrogen with at least a β -chlorethyl functional group markedly lowered respiration. At 0.005% oxygen consumption (given in % was: methopromazine -3, thiopropazine 0, prochlorpromazine 3, acetopromazine 4, chlorpromazine 10, levomepromazine 14, promethazine 16 and alimemazine 28. At 0.02%, the corresponding figures were: thiopropazine -30, methopromazine -31, promethazine -46, levomepromazine -48, acetopromazine -50, prochlorpromazine -50, chlorpromazine -52 and alimemazine -54.

Ecole de Médecine et de Pharmacie
Grenoble, Switzerland

2448 Key, B.J., & Marley, E. The effect of the sympathomimetic amines on behaviour and electrocortical activity of the chicken. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 90-105.

Behavior was recorded concomitantly with cerebral electrical activity from chronically implanted cortical electrodes in 4 chickens. A high correlation was observed between electrocortical activity and behavior, and several of the sympathomimetic amines were administered to observe alterations in either variable. Epinephrine

evarterenol, isoprenaline, etc. produced electrocortical slow wave activity and sleep resembling those produced by pentobarbital. Electrocortical and behavioral sleep was also elicited by metanephrine and nor-metanephrine. Pipadrol regularly elicited behavioral and electrocortical sleep. Amphetamine, methyl phenidate or phenmetrazine produced dual arousal from the 1st day of life. By the 4th week of life, chicks responded to sympathomimetic amines with a transitional electrocortical pattern. At 6 months, almost all amines produced comprehensive alerting. Nicotine produced low-wave activity in young chicks with superimposed spikes.

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2449 Kusch, T., & Heinrich, I. Zur Beeinflussung der Leucin-aminopeptidase durch Phenothiazine und andere Stoffe. [Effect of phenothiazine and other drugs on leucine-aminopeptidase.] *Acta Biologica et Medica Germanica*, 1962, 8, 538-542.

Daily s.c. administration of 1.25 mg/100 g chlorpromazine, thianthene or prothazine to rats did not change the activity of serum leucine-aminopeptidase. The activity was found to be temporarily reduced 4 hours after a single injection. Each of the drugs reduced enzymatic activity in vitro proportional to the dose.

Institut für Pharmakologie
Friedrich-Schiller-Universität
Jena, Germany

2450 Boissier, Jacques-R., Ratouis, Roger, Dumont, Claude, & Pagny, Jeannette. Action dépressive de quelques carbamates de phényl-propa (é) nol au niveau du système nerveux central. [The depressive action of some phenyl-propa (e) nol carbamates at the level of the central nervous system.] *Thérapie*, 1962, 17, 713-718.

The properties of phenylpropyl alcohol carbamates and phenylpropenol (7 compounds) were studied in mice, rats and rabbits. Non-substituted phenylpropanol carbamate is the

most active as a muscle relaxant. Trans-cinnamyl carbamate produced permanent excito-motor syndrome, while cis-cinnamyl carbamate had only sedative action.

Faculté de Médecine
Paris, France

2451 Kusch, T., Heinrich, I., & Hofmann, H. Der Einfluss von Metrazol auf die Dynamik der Ascorbinsäure bei Ratten. [Effect of Metrazol on ascorbic acid metabolism of rats.] *Acta Biologica et Medica Germanica*, 1962, 8, 538-542.

Pentetrazol (Metrazol; 5 mg/100 g) was administered s.c. to mature rats, producing convulsions. The animals were decapitated 1 hour later and the ascorbic acid content of adrenals and liver determined. The ascorbic acid content of the liver did not change, while that of the adrenals rose from ca. 2838 µg/g to ca. 3596 µg/g.

Institut für Pharmakologie
Friedrich-Schiller-Universität
Jena, Germany

2452 Truitt, Edward B., Duritz, Gilbert, Morgan, Ann M., & Prouty, Richard W. Disulfiramlike action produced by hypoglycemic sulfonylurea compounds. *Journal of Studies on Alcohol*, 1962, 23, 197-207.

Male rats received tolbutamide and chlorpropamide (65-250 mg/kg i.p.) 1 hour before ethanol injection (1 g/kg i.p.) to determine the resultant disulfiramlike increase in blood acetaldehyde. Cats and dogs received epinephrine (1 µg/kg i.v.), tolbutamide (200-250 mg/kg i.v.), chlorpropamide (250 mg/kg i.v.), disulfiram (100-250 mg/kg/day for 3 days), calcium carbimide (25 mg/kg p.o.) and insulin (5 U/kg i.v.) at various intervals. Tolbutamide produced markedly increased blood acetaldehyde levels in rats. The vasopressor phase of blood pressure response in cats injected with acetaldehyde was deeper by an average of 16.4 mm, whereas a similar response to epinephrine was unchanged by tolbutamide. Insulin failed to alter the response to acetaldehyde or epinephrine, but a dose of glucose sufficient

to correct the hypoglycemia reversed the tolbutamide-induced potentiation of the hypotensive phase. Bradycardia of vagal origin occurred during the depressor phase of acetaldehyde after tolbutamide injection. Chlorpropamide also actively potentiated acetaldehyde vasodepression. The cardiovascular changes appear to be caused by interference with some glucose dependent function which is affected by tolbutamide but not by insulin.

Department of Pharmacology
University of Maryland School of Medicine
Baltimore, Md.

2453 Melson, F. Weitere pharmakologische Untersuchungen einiger Derivate des 1,3-Dioxolans. II. [Further pharmacological investigations of some derivatives of 1,3-dioxolan. II.] *Acta Biologica et Medica Germanica*, 1962, 8, 381-386.

K 161 (2-p-chlorophenyl-2-methyl-4-hydroxymethyl-1-3-dioxolan; 100-200 mg/kg) potentiates the hypnotic effect of barbiturates in mice. It diminishes the mortality due to administration of strychnine, pentetrazol and picrotoxin and diminishes aggressive behavior among male mice; this latter effect is slightly less than that of meprobamate. It reduces anxiety of rats exposed to electroshock to the same degree as meprobamate. K 161 is considered a tranquilizing agent.

Institut für Pharmakologie
Friedrich-Schiller-Universität
Jena, Germany

2454 Hodes, Robert. Electrocortical synchronization resulting from reduced proprioceptive drive caused by neuromuscular blocking agents. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 220-232.

Gallamine (2-4 mg/kg i.v.) produced electrocortical synchronization in 24 cats which was maintained for many hours. Cessation of gallamine results in rapid synchronization of desynchronized brain potentials with injection of minute amounts (0.25-0.50 mg/kg) of barbiturate. Synchronization

is accompanied by sleep while desynchronization coincides with arousal. Since intra-carotid gallamine injection fails to produce synchronization, cortical synchronization is believed to occur as the result of withdrawal of proprioceptive impulses to the cortex. Such partial deafferentation results in a level of afferent supply insufficient to maintain the brain in a vigilant state.

Department of Pediatrics
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New York, N.Y.

2455 Förster, W., & Kunze, M. Der Einfluss von Iproniazid auf die antiemetische Wirkung von Rauwolfia-Alkaloiden, Tetrabenazin und Chlorpromazin. [The effect of iproniazid on the antiemetic action of Rauwolfia alkaloids, tetrabenazine and chlorpromazine.] *Acta Biologica et Medica Germanica*, 1962, 8, 453-463.

Vomiting was induced by apomorphine (0.015-0.15 mg/kg i.m.) in dogs and cats. The modifying effect of the following drugs administered in a single i.m. injection was investigated: reserpine (0.15-0.5 mg/kg), rescinnamine (1-2 mg/kg), tetrabenazine (40 mg/kg), Raubosin (5-10 mg/kg), and chlorpromazine (1.5 mg/kg). Reserpine and rescinnamine produce vomiting. This effect is noticeable 2 hours after injection, maximal after 24 hours, and extends over a period of 8-10 days. Tetrabenazine suppresses vomiting completely, or almost completely, from 1 hour to 9 days after administration. Raubosin showed similar effects as reserpine for 5-6 days. Chlorpromazine was maximally effective after 2 hours, lasting 24-48 hours. Iproniazid (1000 mg/kg) injected i.p. 24 hours prior to the administration of these drugs counteracted the antiemetic effect of reserpine but not of any of the other drugs. Side effects seen with most of these drugs were apathy, diarrhea, trembling, ataxia and loss of equilibrium. Chlorpromazine produced sedation and ataxia. Three out of 6 dogs which had received 0.25-0.5 mg of reserpine died, and 3 out of 4 cats which received tetrabenazine died.

Pharmakologisches Institut
Medizinische Akademie Magdeburg
Magdeburg, Germany

2456 Förster, W., & Günther, E. Die Beeinflussung des Apomorphinerbrechens durch Pervitin, Iproniazid und Catecholaminvorstufen. [The effect of Pervitin, iproniazid and catecholamine precursors on vomiting induced by apomorphine.] *Acta Physiologica et Medica Germanica*, 1962, 8, 464-471.

Iproniazid (100 mg/kg i.p.) produced vomiting in dogs and intensified the vomiting effect of threshold doses (0.02-0.08 mg/kg i.p.) of apomorphine. Tritophane (100 mg/kg i.p.) and 5HTP (10-50 mg/kg) markedly potentiate vomiting after administration of threshold doses of apomorphine, more so than tyramine (20 mg/kg) or DOPA (30 mg/kg). Vomiting induced by larger dosages of apomorphine (0.1 mg/kg) is greatly reduced (90%) by methamphetamine (1.0 mg/kg), an effect which can be prevented by iproniazid (100 mg/kg i.p.). The antiemetic effect of chlorpromazine was not diminished by iproniazid. The possible central mechanism of these effects is discussed.

Pharmakologisches Institut
Medizinische Akademie Magdeburg
Magdeburg, Germany

2457 Ankermann, Horst. Die Wirkungen des Adrenalin, Noradrenalin und Isoproterenol auf den Gasaustausch und die Körpertemperatur narkotisierter Ratten bei intravenöser Dauerinfusion. [The effects of intravenous infusion of adrenalin, noradrenalin and isoproterenol on oxygen- and carbon dioxide metabolism and on body temperature of anesthetized rats.] *Acta Physiologica et Medica Germanica*, 1962, 8, 489-510.

Fasting anesthetized rats were infused i.v. with epinephrine, levarterenol (adrenalin, noradrenalin) or isoproterenol. Oxygen consumption was accelerated 100% with ca. 1 μ g of each of these drugs. A slightly delayed rise in body temperature accompanied the increase in O_2 consumption. Infusion of 2.8-4.6 μ g of epinephrine or levarterenol produced brief and irregular increase of O_2 utilization up to 200% followed by death. Administration of isoproterenol up to 38.7 μ g did not elevate oxygen consumption above

the 1 γ level, showed no lethal effect, was not abolished after pancreatectomy, and did not elevate blood pressure. No significant changes in respiratory quotient were seen, with the exception of temporary reduction immediately at the start of epinephrine or levarterenol infusion.

Institut für Pharmakologie und Toxikologie
Humboldt-Universität
Berlin, Germany

2458 Flanagan, T.L., Reynolds, L.W., Novick, W.J., Lin, T.H., Rondish, I.M., & Van Loon, E.J. Biliary and urinary excretion patterns of chlorpromazine in the dog. *Journal of Pharmaceutical Sciences*, 1962, 51, 833-836.

In bitches, 200 mg chlorpromazine dissolved in 10 ml of saline was administered intraduodenally by cannula. Bile samples were obtained at 1-hour and urine samples at 2-hour intervals for a period of 8-10 hours following drug administration. Each sample was analyzed individually for "free" and "bound" chlorpromazine and chlorpromazine sulfoxide by the method of Flanagan et al. (1959). In other experiments the dogs received 200 mg chlorpromazine/day p.o. for 2-14 days. Also chlorpromazine (25 mg per kg) containing about 60 μ C of S^{35} was injected into the duodenum and urine samples collected. Based on chromatography and UV analysis, chlorpromazine and its sulfoxide undergo 2 types of binding. Strong alkaline treatment hydrolyzed 1 type while treatment with β -glucuronidase hydrolyzed both types. In urine the concentration of the bound phenothiazines liberated by alkaline hydrolysis was 2-3 times as great as the free material. In bile, the concentration of this type of bound chlorpromazine and chlorpromazine sulfoxide was 10-15 times greater than the free forms of the compound.

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2459 Bircher, Rudolf P., Kanai, Tatsuya, & Wang, S.C. Intravenous, cortical and intraventricular dose-effect relationship of pentylenetetrazol, picrotoxin and deslano-

side in dogs. Electroencephalography and Clinical Neurophysiology, 1962, 14, 256-267.

The dose-route-effect relationship of 0.5-10 mg/kg pentetrazol, 0.5-2000 µg/kg picrotoxin and 1-300 µg/kg deslanoside administered i.v., subarachnoidally on the cortex, in the lateral ventricle, the 3rd and 4th ventricles, was determined in dogs with cannula or catheter chronically implanted in various brain areas. Pentetrazol and picrotoxin produced EEG convulsive discharges when given i.v., cortically or intraventricularly. Pentetrazol acted most rapidly and picrotoxin least rapidly. Deslanoside produced convulsive discharges only when applied cortically or intraventricularly. Cardiac arrhythmias were produced with all 3 drugs, as was an increase in blood pressure accompanied by tachycardia.

Department of Pharmacology
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New York, N.Y.

2460 Stumpf, Ch., Petsche, H., & Gogolak, G. The significance of the rabbit's septum as a relay station between the midbrain and the hippocampus. II. The differential influence of drugs upon both the septal cell firing pattern and the hippocampus theta activity. Electroencephalography and Clinical Neurophysiology, 1962, 14, 212-219.

Septal cell activity and hippocampal EEG's were studied in 15 unanesthetized, curarized rabbits treated i.v. with 0.25 mg/kg eserine, 30 mg/kg hexobarbital, 3 g/kg urethane, 0.1 mg/kg LSD, 0.5 mg/kg scopolamine and 3-6 mg/kg nicotine. Eserine and nicotine induced β -units in the septum to discharge in bursts which were synchronous with the hippocampal theta waves. Low doses of hexobarbital and scopolamine diminish theta rhythm and burst frequency of β -units, while high doses abolish theta rhythm and replace regular burst pattern with an irregular firing pattern, indicating depression of the limbic subcortical regions. LSD acts directly on the hippocampus, abolishing theta rhythm without

changing the septal burst activity. Urethane, hexobarbital and scopolamine effect a incomplete depression of the subcortical limbic centers coupled with a direct effect upon the hippocampus.

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University of Vienna
Vienna, Austria

2461 Lester, David. The concentration of apparent endogenous ethanol. Quarterly Journal of Studies on Alcohol, 1962, 23, 17-25.

Alcohol disappearance was measured by analysis of alveolar air by gas-liquid chromatography in 3 people who drank 0.2-0.6 g/kg. Alveolar air samples from 1 nonalcoholics and 6 alcoholics were also analyzed. No differences were noted in ethanol concentrations between alcoholics and nonalcoholics. No alcohol was detectable in 10, 7 showed a concentration of 0.5 mg/liter blood, 5 showed 1.0 mg/liter and 3 manifested 1.5 mg/liter. Direct determinations of the rate of ethanol disappearance at concentrations below 100 mg per liter serum reveal a linear rate of disappearance up to 50 mg/liter. Exposure of 6 people to simulated attitudes of 4000 for 1-2 hours and 4 rats to 7000 mg for 4 hours did not produce any increase in alcohol concentration. Ethanol concentration in rat liver was 9 mg/1000 g, while 1/10 these values were obtained in the living animal with peritoneally equilibrated nitrogen. Ethanol, which may or may not be of endogenous origin, is present in human beings in concentrations up to 1.5 mg per liter of blood.

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2462 Barth, H., Gebhard G., Kiesewetter R., & Mütler, M. Dämpfende Eigenschaft einiger 3,4,5-Trimethoxybenzoylderivate. 2. Mitteilung. [Quieting properties of certain 3,4,5-trimethoxybenzoyl derivative. Part 2.] Pharmazie, 1962, 17, 351-355.

Five substances were reported: N-ethyl

N-3,4,5-trimethoxybenzoylurea (ETBH), N-butyl-N-3,4,5-trimethoxybenzoylurea (or BTBH), 3,4,5-trimethoxybenzoylbutylamide (BTBA), Trimeglamide, Adalin carbromal or which the LD₅₀, ED₅₀, and SD₅₀ (dosage at which the animals assume lateral decubitus) were determined. Test animals for the above determinations were mice, rats and trapped wild rats. Administration was oral, in the form of a 2% aqueous solution of gum arabic. Dosages of 50 and 100 mg/kg ETBH and 100 mg/kg BTBH p.o. resulted in pronounced sedation in cats, for 24-hour periods. Somnolence was obtained with 225 mg/kg BTBH. Side effects included tremor, tachycardia, salivation, and reduced muscle tone. IDPN-induced hypermotoricity in mice was reduced to the 50% level by 1.8-5.5% of the LD₅₀ doses of the above drugs. Dosages of 5-19% of the LD₅₀, reduced by 1/2 the ability to maintain equilibrium in a rotarod test. The drugs are only mildly antagonistic to electric shock at 1.4-7% of the LD₅₀. ETBH (10-40 µg/ml), BTBH (5-10 µg/ml) and BTBA (25-50 µg/ml) reduced the combat drive of Siamese fighting fish. The same compounds reduced anxiety symptoms in rats.

EB Arzneimittelwerk
Hresden, Germany

2463 Driver, M.V. A study of the photoconvulsive threshold. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 359-367.

The photoconvulsive threshold was determined by administering 5% pentetrazol or 5% hexazole (5-40 mg/kg) to 77 patients (3 epileptics, 22 schizophrenics and 32 depressives), after which height, weight, surface area, body type, blood sugar and hemoglobin levels were measured. Blood and plasma volume and cardiac output were also measured in 48 patients. No relationship was established between sex, age, body type, blood sugar and hemoglobin as opposed to convulsive threshold. Body size determined drug dosage. Arterial concentration calculated at the end point provided a satisfactory means of separating subcortical epileptics from other subjects. Photoconvulsive EEG end-points were

manifested by 75% of the epileptics, 40% of the schizophrenics and 6% of the depressives.

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Institute of Psychiatry
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London, Great Britain

2464 Wada, Toyoji, Goto, Akira, & Fukushima, Yutaka. Megimide-metrazol (M-M) activation in clinical electroencephalography. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 408-410.

A megimide (90 mg)-pentetrazol (metrazol) (200 mg) activation technique (4 cc i.v. followed by 1 cc every 15 seconds for 1 minute and 30 seconds) was combined with routine photic stimulation, after which 1 cc was injected every 15 seconds during light flashing procedures in 103 epileptics, 58 schizophrenics and 57 neurotics. Positive activation constituted a burst of abnormal discharges during seizure activity. Positive results were obtained in 95% of the epileptics, 55% schizophrenics and 46% of the neurotics. Differences between epilepsy and schizophrenia or neurosis are very significant. The average threshold value for megimide-pentetrazol activation in epilepsy in about 0.2 cc/kg in comparison with that for megimide (0.9 mg/kg) and for pentetrazol (2.0 mg/kg). With pentetrazol-photic activation the average threshold was as follows: 5.4 mg/kg in epilepsy, 6.1 mg/kg in schizophrenia and 6.8 mg/kg in neurosis. Following bursts of abnormal discharges clinical seizures were produced in 58 epileptics. Side effects included nausea, facial congestion, palpitation, dizziness, flushing, tremor, vomiting, tinnitus and pain in the extremities. The technique appears efficacious.

Department of Neuropsychiatry
Hirosaki University School of Medicine
Hirosaki, Japan

2465 Selldén, Ulla. The role of hyperventilation in the initial electroencephalographic responses to activation with megimide. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 368-375.

In conjunction with EEG studies, 12 people (9 normal, 1 epileptic, 1 amnesiac and 1 with multiple sclerosis), aged 20-51 years, received PCO_2 determinations in arterial blood (PaCO_2) at rest and during megimide (40-150 mg i.v.) activation. PaCO_2 determinations were also made during and after voluntary hyperventilation in 10 subjects, to establish whether hyperventilation might be implicated in initial EEG response to megimide activation. A slight rise in ventilation accompanies megimide activation. Since this response is not significant, it may be ignored as a source of error when initial EEG responses to megimide activation are evaluated.

Laboratories for Clinical Physiology and
Clinical Neurophysiology
Sahlgrenska Sjukhuset
Göteborg, Sweden

2466 Kanai, Tatsuya, Misrahy, George, & Clark, Leland C. Neuropharmacological effects of O-methylbufotenine. Federation Proceedings, 1962, 21, 322. [Abstract]

Minutes after the injection of 0.5 mg/kg parenteral or intraventricular injections of 5 μ /kg O-methylbufotenine cats are apprehensive, show autonomic overactivity, ataxia, catatonicleike postures and mixed reactivity to sensory stimuli. These effects are reduced by lobotomy, section of optic nerves, tranquilizers and anesthetics. Decortication or decerebration suppresses hyperventilation. EEG shows high amplitude slow waves and increased arousal responses. Cortical evoked responses to sensory stimuli increase; threshold of mid-brain to electrical stimuli drops; and cochlear threshold and behavior of Purkinje cells do not change significantly. Response to pain is diminished. Small doses induce tachycardia and increase blood pressure; large doses cause the opposite effect. Pressor responses are elicited by tactile and sound stimuli, but not by pain. Bufotenine, in conjunction with methionine, may induce changes similar to O-methylbufotenine.

Memorial Childrens Hospital
Los Angeles, Calif.

2467 Wylie, David W., & Archer, S. Tranquilizing activity of a series of indole alkyl phenylpiperazines. Federation Proceedings, 1962, 21, 322. [Abstract]

Indole alkyl phenylpiperazines possess the properties of major tranquilizers but differ in some important aspects. In general this type of agent potentiates hexobarbital, reduces aggressiveness in monkeys, causes catalepsy, reduces spontaneous activity in mice, does not protect against chemically or electrically induced convulsions and depresses the head-withdrawal reflex, is adrenolytic, antiemetic and weakly antihistaminic. The structure lends itself to wide chemical variations; some compounds in this group possess important differences from phenothiazines in use. One compound, 1-2-[(2-methyl-3-indolyl) ethyl]-4-phenylpiperazine has no cataleptogenic activity up to toxic doses, although it is as active as chlorpromazine in potentiating hexobarbital and reducing spontaneous activity in mice. Another, 1-(2-anisyl)-4-[2-(5,6-methylenedioxy-3-indolyl)-ethyl] piperazine (Solypertine), is less active than chlorpromazine in potentiating hexobarbital and in producing catalepsy, but is 3 times more active as an adrenolytic agent. Another, 1-[2-(5,6-dimethoxy-2-methyl-3-indolyl) ethyl]-4-phenylpiperazine (oxyperotine), has the central properties of chlorpromazine, but is 3-4 times as active and only 1/2 as adrenolytic.

Sterling Winthrop Research Institute
Rensselaer, N.Y.

2468 Björnesjö, K.B., & Jarnulf, B. Determination of iproniazid and nialamide in blood serum and urine. Scandinavian Journal of Clinical and Laboratory Investigation 1962, 14, 408-415.

With sodium nitritopentacyanoferroate, iproniazid and nialamide give colored reaction products which can be used for quantitative analysis. Concentrations above 10 μ g/ml can be determined quantitatively at 440 m μ . Supplementary paper chromatography was used for the identification of possible interfering substances.

Central County Hospital of Karlstad
Karlstad, Sweden

2469 Monnier, Marcel, & Romanowski, W. Les systèmes cholinocéptifs cérébraux—actions de l'acétylcholine, de la physostigmine, pilocarpine et de GABA. [Cerebral cholinocceptive systems—actions of acetylcholine, physostigmine, pilocarpine and GABA.] *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 486-500.

Rabbits were stereotaxically implanted with electrodes according to the method of Monnier and Gangloff (1961), allowing experimentation with the awake animal. Both spontaneous and evoked potentials were studied. Injection of drugs was made into the carotid artery except for atropine which was injected into the marginal ear-vein. Acetylcholine (0.0004-0.003 mg/kg), physostigmine (0.035-0.1 mg/kg), pilocarpine (0.07-0.33 mg/kg) and GABA (0.2-0.5 mg/kg) were used. The following electrophysiological alterations were noted: a/ arousal syndrome characterized by desynchronized electrical activities in the neocortex with synchronization taking place in the hippocampus, caudate nucleus and reticular system; b/ increased arousal reaction to sensory and reticular stimuli; c/ slightly increased cortical potentials evoked by stimulation of the reticular system; d/ markedly increased cortical potentials evoked by stimulation of the hippocampus and caudate nucleus; e/ decreased recruiting potentials evoked by stimulation of the medial thalamus, and f/ unaltered or slightly decreased cortical potentials evoked by ventrolateral thalamus stimulation. Most of these effects were suppressed by atropine. The existence of cholinocceptive substrates inhibiting synchronization in the neocortex, and of cholinocceptive substrates facilitating synchronization in the hippocampus and caudate nucleus are proven. The action of GABA is often similar to that of acetylcholine and other parasympathomimetic drugs.

Institut de Physiologie
Université de Bâle
Basel, Switzerland

2470 Roux, G., Rouffiac, R., Costes, J., & Dumas, J.C. Etude expérimentale de l'influence du méprobamate sur le fonctionnement hépatique. [Experimental study

on the influence of meprobamate on hepatic function.] *Thérapie*, 1962, 17, 303-310.

Dogs were given massive doses of meprobamate, 0.10-0.15 g/kg (about 3 times the maximal therapeutic dose equivalent to 9 g per day in man) for 3 months. This dosage was then established as the approximate threshold limit for liver tolerance.

Université de Toulouse
Toulouse, France

2471 Clifford, Donald H., Good, Archie L., & Stowe, Clarence M. Observations on the use of ataractic and narcotic pre-anesthesia and pentobarbital anesthesia in bears. *Journal of the American Veterinary Medical Association*, 1962, 140, 464-470.

Intramuscular injection of large doses of promazine (8.8 mg/kg) and pethidine (22 mg per kg) were not effective preanesthetics in the North American bear. Morphine (4.4 and 8.8 mg/kg i.m.) was effective prior to pentobarbital anesthesia. Promazine (4.4 and 8.8 mg/kg) potentiated morphine. Suggested doses are 8.8 mg/kg morphine and 4.4 mg/kg promazine.

Division of Veterinary Surgery and
Radiology
College of Veterinary Medicine
University of Minnesota
St. Paul, Minn.

2472 Casier, H. Accumulation of alcohol metabolites in the form of total lipids and fatty acids in the organism. *Quarterly Journal of the Studies on Alcohol*, 1962, 23, 529-548.

Groups of mice were given injections of 0.3, 0.6, 0.9 ml of a 33% alcohol solution, corresponding in radioactivity to 1.2, 2.4 and 3.6 μ c. The amounts of alcohol were correspondingly 1.25, 2.5 and 3.75 g/kg. For comparison of the fixation of alcohol metabolites with that of sodium acetate equimolar doses of alcohol and acetate were injected. When a daily dose of 0.3 ml alcohol was administered for 8, 15 and 21 days respective amounts of alcohol metabolites reached 3-6 times as high a value

as after the administration of a single dose. Probably a condensation or combination occurs between acetaldehyde and acetyl CoA with the formation of cholesterol and lipids. Hence the origin of the fixed metabolites derived from alcohol should be different from the origin of fixed metabolites derived from acetic acid.

Institut J.F. Heymans de Pharmacodynamie
Ghent, Belgium

2473 Cadell, T.E., Harlow, H.F., & Waisman, H.A. EEG changes in experimental phenylketonuria. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 540-543.

Five rhesus monkeys were raised from the 5th day of life on a diet of whole cow's milk or powdered milk which contained 0.25 g phenylalanine/100 ml. After 2 weeks the concentration was increased to 0.5 g phenylalanine/100 ml. Daily intake was ca. 2.75 g. Electrodes were implanted and recordings made with the animals restrained in a supine position. A photostimulator was used. The predominance of slow activity in the phenylketonuric (PKU) monkey seems to agree partially with EEG findings in humans with phenylketonuria. Slow activity is not constant, merely predominant. Ordinarily EEG's contain 3/ second spikes and waves. Sleep was induced in 3 PKU monkeys by 50 mg/kg amobarbital i.p., and records taken in sleep did not show any petit mal type discharge. Two of the 5 animals have had grand mal seizures with tonic-clonic contractions in all extremities. PKU animals had a reduced following response to photic stimulation and showed a trend toward greater deficits in following with increasing age.

Department of Psychology
University of Wisconsin
Madison, Wis.

2474 Dat-Xuong, N., Duchêne-Marullaz, Vacher, J., & Buu-Hoi, N.P. Activité antimonoamineoxydase de divers dérivés des nicotiny- et isonicotinyldiazines. [Antimonoamine oxydase activity of various nicotiny- and isonicotiny- hydrazines.]

Medicina Experimentalis, 1962, 7, 85-91.

Twenty-two hydrazine derivatives were investigated for MAO inhibition and 6 proved active, but less active than iproniazide. LD₅₀'s, ED₅₀'s and MAO inhibition were reported for mice.

Institut de Chimie des Substances
Naturelles du CNRS
Gif-sur-Yvette, France

2475 Valette, G., & Massé, Chr. Effets synergiques et antagonistes de divers agents sympathomimétiques dérivés de la phényl-isopropylamine à l'égard de l'adrénaline. Etude sur la vésicule séminale du rat. [Synergistic and antagonistic effects of various sympathomimetic derivatives of phenylisopropylamine in relation to epinephrine (adrenalin). Study on the seminal vesicle of the rat.] *Journal de Physiologie*, 1962, 54, 420-421.

Dose-effect curves were established for sympathomimetic effect on the isolated rat seminal vesicle at a fixed 2 µg/10 ml epinephrine level for 0-1000 µg/ml of amphetamine, methamphetamine, norephedrine and ephedrine. Maximum contractions were obtained with amphetamine and methamphetamine at 5 µg, norephedrine 10 µg and ephedrine 25-50 µg.

Laboratoire de Pharmacodynamie
Faculté de Pharmacie
Paris, France

2476 Buchel, Laia, & Lévy, Jeanne. Phénomènes d'antagonisme et de synergie appliqués à l'étude pharmacologique de divers neuroleptiques. [Phenomena of antagonism and synergism applied to the pharmacologic study of various neuroleptics.] *Journal de Physiologie*, 1962, 54, 304-305.

Chlorpromazine (1 and 2 mg/kg), reserpine (0.75 mg/kg) and triperidol (0.1 mg/kg) were tested in Swiss mice against amphetamine, caffeine and cocaine. Their synergistic effects were determined in potentiation of chloral hydrate (375 mg/kg i.p.) sleep. At doses which do not produce significant action in normal animals, the

neuroleptics antagonize amphetamine, caffeine and codeine. Only triperidol showed synergism which prolonged chloral hydrate sleep.

Laboratoire de Pharmacologie Chimique
Faculté de Médecine
Paris, France

2477 Hashimoto, P.H., Maeda, T., Torii, K., & Shimizu, N. Histochemical demonstration of autonomic regions in the central nervous system of the rabbit by means of a monoamine oxidase staining. Medical Journal of Osaka University, 1962, 12, 425-439.

Fresh frozen serial sections of the brain and spinal cord of 5 healthy adult animals were incubated in the following mixture for 45 minutes at 37°C: 25 mg tryptamine HCl, 4 g Na₂SO₄, 5 mg nitro-BT (2,2'-p-dinitrophenyl-5,5'-diphenyl-3,3'-(3,3'-dimethoxy-4,4'-diphenylene) ditetrazolium HCl), 5 ml 0.1 M phosphate buffer and 5 ml distilled water. After formalin fixation staining was made with Klüver-Barrera's (1953) method or gallocyanin. MAO activity in the CNS was found fairly specific to autonomic regions.

Department of Anatomy
Osaka University Medical School
Osaka, Japan

2478 Delost, P., & Prulhière. Réserpine et croissance. [Reserpine and growth.] Journal de Physiologie, 1962, 54, 322-323.

Female Swiss mice (21-29 days of age) were divided into 4 groups and given reserpine (mg/kg/day) as follows: 1, 0.25, and 0.5 for 8 days (sacrificed on the 9th day) and 0.50 every 2nd day for 15 days (sacrificed on the 16th day). They were all sacrificed at 37-38 days of age. Reserpine injected each day in doses from 0.25-1 mg/kg for 8 days stopped weight growth completely and produced a diminution in terminal weight. Injection of 0.5 mg/kg reserpine every 2nd day slowed without inhibiting weight development. Body measurements in relation to controls were much smaller after daily treatment with

reserpine 1 mg/kg for 8 days. Injection of reserpine causes profound sleep for 15-20 hours, diminishing considerably the opportunity for feeding. Growth inhibition is merely parallel to degree of inability to feed.

Laboratoire de Physiologie Animale
Faculté des Sciences
Clermont-Ferrand, France

2479 Higuchi, Hideo, Matsuo, Takaaki, & Shimamoto, Kiro. Effects of methamphetamine and cocaine on the depletion of catecholamine of the brain, heart and adrenal gland in rabbit by reserpine. Japanese Journal of Pharmacology, 1962, 12, 48-56.

One mg/kg methamphetamine or 2 mg/kg cocaine was injected i.v. 1 hour before the administration of 1 mg/kg reserpine in intact rabbits. Brain, heart and both adrenals were taken and their homogenates assayed for epinephrine and levarterenol. Both drugs depressed the levels of catecholamine in central and peripheral organs, the effect being more marked in the brain tissues. During the decrease of central catecholamines, the animal showed motor and sympathetic excitement. The i.v. injection of 1 mg/kg to rabbits pretreated with 1 mg/kg methamphetamine reestablished levarterenol brain content in the 1st half hour of reserpine administration. During this reestablishment, the animal showed motor excitement. When the same reserpine treatment was applied following cocaine, levarterenol in brain tissue did not become reestablished, but decreased sharply. A similar decrease of catecholamine was observed in the atria and adrenal glands.

Department of Pharmacology
Faculty of Medicine
Kyoto University
Kyoto, Japan

2480 Tuchmann-Duplessis, H., Gabe, M., & Mercier-Parot, L. Diminution du produit de sécrétion hypothalamo-neuro-hypophysaire après injection de réserpine. [Diminution of hypothalamo-neuro-hypophyseal secretory product after reserpine in-

jection.] *Annales d'Endocrinologie*, 1962, 23, 65-77.

Histology of the hypothalamo-hypophyseal neurosecretory path in rats after 50-75 μ g per day reserpine for 1-10 days revealed a reduction in neurosecretory production (using fuchsin-paraldehyde). This did not appear related to electrolyte balance. Evidence favors direct action for reserpine on the hypothalamo-hypophyseal complex.

Laboratoire d'Embryologie
Faculté de Médecine
45, rue des Saints Pères
Paris, France

2481 Ochs, S., Dowell, A.R., & Russell, I.S. Mescaline convulsive spikes triggered by direct cortical stimulation. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 872-884.

The cortices of rabbits and cats were exposed after anesthesia; stimulating pulses were applied with bipolar electrodes. Mescaline (a small drop of 1% solution placed on the cortex at the site of the recording electrode) was effective in producing convulsive activity in both the intact cortex and in cortical island preparations. Driven spikes were found in a number of cortical regions, including frontal regions of the rabbit and suprasylvian gyrus of the cat, in addition to the visual cortex of the rabbit. Spikes could be elicited in the acute and chronic cortical island preparations. The latency of the spike may be short and the response gives the false appearance of an exaggerated direct cortical response (DCR) or the latency may be longer than 100 milliseconds varying with stimulus strength. The DCR usually decreases in size after mescaline application and does not appear to be casually related to the spike. GABA rapidly blocks both the DCR and the spike, producing an inversion of the DCR, but not the spike. Mescaline spikes can be blocked by i.v. pentobarbital, while DCR remains. Direct intracortical action of pentobarbital to depress mescaline-sensitized intracortical neurons is thereby indicated.

Indiana University School of Medicine
Indianapolis 7, Ind.

2482 Kajtor, F., Veres, Olivia, & Kocsár, L. Effect of protracted meprobamate treatment on the bioelectric and phosphorylase activity of the dog brain. *Acta Medica*, 1962, 18, 373-384.

Various doses of meprobamate were administered to dogs for 7-21 days. In addition to the tranquilizing effect, it caused slowing of brain rhythms and/or the appearance of β -spindles. Meprobamate treatment in 13 animals was followed by a decrease in cerebral phosphorylase activity. Compared to those of controls, mean values decreased to 19% in the cortex, 21% in the pyriform lobe and 31% in the thalamic-hypothalamic area. No regular correlation between extent of endomatic inhibition and degree of bioelectric synchronization demonstrated. Some animals developed a high tolerance to meprobamate. The drug appears to inhibit the connection to the reticular structures in the upper brain-stem and thalamus with the cortex and the hippocampal formation, although its cortical effect is not negligible.

Department of Neurology and Psychiatry
University Medical School
Debrecen, Hungary

2483 Bradley, P.B., & Nicholson, A.N. The effect of some drugs on hippocampal arousal. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 824-834.

Encéphale isolé preparations were made from adult cats and the electrical activity of the ventral hippocampus recorded with a concentric bipolar electrode (Bradley and Key 1958.) Atropine (0.25-3.0 mg/kg i.v.), physostigmine (following atropine at 0.4-0.8 mg/kg, up to 1.25 mg/kg), amphetamine (racemic-0.25-2.0 mg/kg i.v.), pentobarbital (1-35 mg/kg i.v.), amobarbital (at slightly higher doses than necessary with pentobarbital) and thiopental (2-4 and 8 mg/kg i.v.) were employed. Amphetamine and pentobarbital induced changes in the hippocampal activity which correlated with the state of wakefulness and sleep whereas atropine and physostigmine used changes which were uncorrelated with behavior. The electrical activation of the hippocampus and neocortex

may be due to an inhibitory control of hippocampal neurons by the midbrain limbic area. The synchronous activity in wakefulness after amphetamine may be due to activation of an inhibitory reticular control exerted by the midbrain limbic area. It is unlikely that changes in hippocampal activity associated with arousal are mediated by a predominantly cholinergic system.

Medical Research Council Neuropharmacology
The Medical School
Birmingham 15, Great Britain

2484 Schwartz, Marvin, Shagall, Charles, Bittle, Robert, & Flapan, Marshall. Dose related effects of pentobarbital on somatosensory evoked responses and recovery cycles. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 898-903.

Intraperitoneal injections of 5, 10, 15 and 20 mg/kg pentobarbital were given to cats in acute and chronic EEG experimentation. Cortical recordings were obtained from the posterior sigmoid gyrus with the reference in the frontal sinus. Spontaneous and evoked patterns were studied. Although pentobarbital reduced both the amplitude and degree of recovery of the evoked potentials, only the recovery changes during the relative unresponsive period provided a dose-sensitive indicator. Amplitude was affected only by maximal dose levels. The state of alertness and barbiturates probably affect the recovery cycle through mechanisms in the brain-stem reticular formation that are at least partially independent. Low doses of barbiturates probably affect reticular mechanisms which control recovery, and higher doses probably exert an additional depressant action on the thalamic relay nuclei.

Department of Psychiatry
Psychopathic Hospital
State University of Iowa
Iowa City, Iowa

2485 Miquel, I., & Dominguez Mijan, C. Metfendrazina nuevo inhibidor de M.A.O. [Methphendrazine, a new MAO inhibitor.] *Archivos del Instituto de Farmacologia*

Experimental, 1962, 14, 47-59.

The in vitro MAO inhibitory potential of a series of compounds designated HM-, was assayed with rabbit liver homogenates and in vivo MAO inhibition was determined spectrofluorometrically by levarterenol and 5HT concentrations in tissues of rats and mice in acute and chronic trials. Methphendrazine (HM-11) was the best inhibitor, increasing the basal level of amines in vivo. Intravenous methphendrazine did not alter either the hypertensive response of epinephrine, or vasomotor reflexes. In the frog, methphendrazine showed hardly any cardiac reaction. The LD₅₀ in the mouse is 38.7 mg/kg and in the rat 91 mg/kg. Administered to the rat at lethal or sublethal doses, methphendrazine produced restlessness, exophthalmia, hydriasis, tremor, excitability and death by respiratory paralysis. It did not produce hemic, hepatic, renal or pulmonary degeneration nor did it produce anorexia. Spontaneous motility in the rat was increased 30%, against 500% increase for amphetamine. Reserpine stupor in rats was negated by pretreatment with methphendrazine, and tryptamine convulsions were greatly potentiated.

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Instituto de Farmacología Experimental
Sección de Madrid
Madrid, Spain

See also 2255, 2357, 2388, 2398, 2406, 2486, 2488, 2501, 2506, 2531.

2486 Ankermann, Horst. Zum Problem der stoffwechselsenkenden Wirkung des Adrenalin. [The mechanism of the metabolism-reducing action of adrenalin.] *Acta Biologica et Medica Germanica*, 1962, 8, 609-616.

Intravenous infusion with small amounts of epinephrine (adrenalin; 1.5 γ /minute/100 g) into rats increased oxygen consumption and blood pressure. Additional infusion of the sympatholytic phentolamine [2-(N-p-Tolyl-N-m oxygenyl-aminomethyl)-imidazoline] (3 γ /minute/100 g) did not change the accelerated metabolic rate but prevented the rise of blood pressure. Large doses of epinephrine (3.8 γ) reduced the oxygen consumption to about half the norm in 12 out of 16 rats. Simultaneous infusion of phentolamine (7 γ) produced in all (8) rats an almost 2-fold increase in oxygen consumption, although this dosage of phentolamine without epinephrine does not significantly alter the metabolic rate. Also, the metabolic effect may be caused solely by its pressor effect.

Institut für Pharmakologie und Toxikologie
Humboldt-Universität
Berlin, Germany

2487 Schmidt, Joachim, & Matthies, Hans-Jürgen. Über einen zentralen Serotonin-Noradrenalin-Antagonismus. [Central antagonism of serotonin and noradrenalin.] *Acta Biologica et Medica Germanica*, 1961, 7, 107-109.

Injection into the cerebrum of either 5HT (serotonin) or levarterenol (noradrenalin) significantly prolonged duration of hexobarbital anesthesia (100 mg/kg i.p.) in mice. Simultaneous injection of both 5HT and levarterenol slightly shortened the anesthesia. Duration of anesthesia was reduced by injection of 5HT into the cerebellum; this effect was cancelled by the simultaneous injection of levarterenol. Dopamine showed the same effects as levarterenol; DOPA was without influence.

Pharmakologische Institut
Medizinische Akademie Magdeburg
Magdeburg, Germany

2488 Lee, Joseph C. Effect of alcohol injections on the blood-brain barrier. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 4-16.

Of 21 rabbits receiving ethanol injections in the left common carotid artery, 7 got 2 cc of 30% solution, 8 received 2 cc of 7.5-45% solution and 6 received 4-10 cc of 30% solution, after which they were sacrificed at various intervals. Radioautographic studies with radioactive iodinated bovine albumin were used to detect changes in cerebral vascular permeability. The healthy cerebral blood vessels were impermeable to albumin molecules and trypan blue particles. Injections of alcohol produced a transient increase in cerebral vascular permeability to these molecules. Death ensued after injection of 10 cc alcohol solution at greater than 45% concentration. Radioautographs became very intense after 1 hour and declined markedly within 6 hours. Radioactivity was very pronounced in the thalamus, hypothalamus and amygdaloid nuclei, but less so in the cerebral cortex. Spread of radioactivity was observed in the opposite cerebral hemisphere along the corpus callosum, hippocampus and massa intermedia. Apparently alcohol influences neuronal metabolism which in turn produces an alteration in the blood-brain barrier.

Department of Anatomy
University of Saskatchewan
Saskatoon, Saskatchewan
Canada

2489 Holmberg, Maj Britt, & Jansson, Bengt. A study of blood count and serum transaminase in prolonged treatment with amitriptyline. *Journal of New Drugs*, 1962, 2, 361-365.

Amitriptyline (usually 50-100 mg/day) was administered to 100 depressed patients aged 10-79 years for an average of 6.1 months following 2 months pretreatment. Laboratory tests, including SGPT, white blood count and differential counts were performed once a month for the duration of treatment. Of necessity chlorpromazine was administered to 10%. About 84% of the patients showed obvious improvement in

depressive symptoms, even though improvement in 19% was contingent upon continued medication. Optimal responses were obtained with 58.6% of the endogenous depressions and 64% of asthenic-depressive syndromes. With regard to blood changes a single rise in eosinophil count was observed in 38% and a more concrete tendency toward eosinophilic reaction in 11%. Eosinophilia values of 10% were exceeded in only 3 patients. SGPT changes were insignificant, with transient increases observed in only 3 patients.

University Psychiatric Clinic
Sahlgren's Hospital
Göteborg, Sweden

2490 Schmid, E., Witte, S., Pfannmüller, B., & Schrick, K. Th. Über den Einfluss von Prednisolon, Nucleosiden und Aminoxydasehemmern auf die Serotoninbildung alternder Blutplättchen. [The influence of prednisolone, nucleosides and amino oxydase inhibitors on the serotonin-binding capacity of old blood platelets.] *Thrombosis et Diathesis Haemorrhagica*, 1962, 7, 258-272.

The influence of prednisolone, nucleosides and MAO inhibitors on 5HT (serotonin) binding by old thrombocytes in platelet-rich plasma was investigated. In vitro concentrations and substances used were: 0.1 mg/ml prednisolone, 2 mg/ml inosine, 2 mg/ml inosine plus 0.1 mg/ml adenine plus 1 mg/ml pyridoxal, 0.5 mg/ml iproniazid, 0.5 and 0.01 mg/ml nialamide and 1.0 µg/ml 5HT-creatinine sulphate. Prednisolone retards the loss of amines in stored blood platelets and inhibits the decrease of hemic 5HT concentration. Nucleosides do not influence the fixation of 5HT; they block the accumulation of 5HT by thrombocytes. These 2 compounds do not influence platelet survival. MAO inhibitors block the enzymatic degradation of 5HT in plasma; they act as 5HT antagonists and therefore influence the biological assay of amine concentration in various blood fractions. This inhibition is particularly strong in the platelet fraction. MAO inhibitors can be electively fixed by thrombocytes. The therapeutic use of the active agents is discussed.

Medizinische Universitätsklinik Erlangen
Erlangen, Germany

2491 Davis, Charles S., Jenkins, Glenn L., Knevel, Adelbert M., & Paget, Charles. Synthesis of some N- and S-substituted derivatives of 2-aminobenzenethiol. *Journal of Pharmaceutical Sciences*, 1962, 51, 840-842.

Ten N- and S-substituted derivatives of 2-aminobenzenethiol (2-(2'-diethylaminoethylamino) benzenethiol, 2,2-pentamethylenebenzothiazoline, etc.) were prepared by various synthetic techniques as intermediates in the synthesis of analogues of the phenothiazine tranquilizers. A new synthesis for preparing the benzothiazine ring is reported and cleavage of the 2,2-pentamethylenebenzothiazoline ring with alkylating agents is discussed.

Research Laboratories
School of Pharmacy
Purdue University
Lafayette, Ind.

2492 Mellinger, Theodore J., & Keeler, Clyde E. Chromatography and electrophoresis of phenothiazine drugs. *Journal of Pharmaceutical Sciences*, 1962, 51, 1169-1173.

Through separation techniques, electrophoresis, paper chromatography and thin-layer chromatography were used in order to differentiate 19 phenothiazine compounds (chlorpromazine, perphenazine, prochlorperazine, etc.) and 4 similar compounds (imipramine, chlorprothixene, isothypendyl and prothypendyl). Electrophoresis produced fast and distinctive migration of these compounds, but tailing interfered with the usefulness of this technique. Paper chromatography proved to be a valuable and easy means of separating these drugs. Thin-layer chromatography with silica gel showed the most accurate separation of phenothiazine compounds. Chromatography in combination with color reaction or fluorescence permitted good differentiation of the various phenothiazine tranquilizers.

Milledgeville State Hospital
Milledgeville, Ga.

2493 Blake, Martin I., & Siegel, Frederick P. Analysis of phenobarbital elixir by an ion exchange and nonaqueous titration procedure. *Journal of Pharmaceutical Sciences*, 1962, 51, 944-946.

Phenobarbital, secobarbital, amobarbital and pentobarbital elixirs were analyzed by passing an aliquot through a strongly basic anion exchange resin, followed by elution with acetic acid in ethanol. Barbiturate assay was completed by evaporating the solvent, dissolving the residue in dimethylformamide and titrating with sodium methoxide in benzene-methanol. Recovery was far in excess of that obtained with standard procedures.

College of Pharmacy
University of Illinois
Chicago, Ill.

2494 Brochmann-Hanssen, E., & Svendsen, A. Baerheim. Separation and identification of sympathomimetic amines by gas-liquid chromatography. *Journal of Pharmaceutical Sciences*, 1962, 51, 938-941.

Amphetamine, mephentermine, epinephrine, levarterenol and various other sympathomimetic amines were subjected to gas chromatographic analysis on low-loaded columns. All compounds save phenylephrine and synephrine could be separated on a column of silicone rubber SE-30. Many of the amines reacted with ketones to produce sharp, symmetrical peaks on the gas chromatogram. Ephedrine and pseudoephedrine can be separated and identified on the basis of the difference in the rate of reaction with acetone. Certain phenolic amines were difficult to gas chromatograph because of adsorptive effects. Monophenolic amines yielded good chromatograms as ketone derivatives. Catecholamines gave optimal results after acetylation and treatment with hexamethyldisilazane before chromatography.

University of California School of Pharmacy
San Francisco, Calif.

2495 Mabry, C. Charlton, Nelson, Thomas L., & Horner, Frederick A. Occult phenyl-

ketonuria. *Clinical Pediatrics*, 1962, 1, 82-86.

A 6-month old male with a history of negative FeCl_3 and Phenistix urine test was diagnosed as a phenylketonuric on the basis of the following findings: his older sister has phenylketonuria, he has developmental retardation with neurologic findings compatible with phenylketonuria, excess urinary o-hydroxyphenylacetic acid, excess urinary phenylalanine and an abnormally elevated serum phenylalanine. Problems inherent within detection of early phenylketonuria are elaborated.

Department of Pediatrics
University of Kentucky Medical Center
Lexington, Ky.

2496 Luts, Heino A., & Nobles, W. Lewis. New 3-thiophene derivatives as sedative agents. *Journal of Pharmaceutical Sciences*, 1962, 51, 1173-1175.

A group of Mannich bases and their derivatives were synthesized from 3-propionylthiophene for pharmacological evaluation. Preliminary information indicates that 1 of the 8 compounds, 3-dimethylamino-2-methyl-1 (3-thienyl)-1-phenylpropanol hydrochloride, combined sedative and stimulating properties "in a most interesting manner."

School of Pharmacy
University of Mississippi
Oxford, Miss.

2497 Bonta, I.L., Wijmenga, H.G., & Hohensee, F. The action of Substance P and other brain extracts on the central nervous system. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 265. [Abstract]

CNS depressant activity of crude preparations containing Substance P could be confirmed, using the exploratory behavior-test and i.v. strychnine titration. However, other subfractions of hog-brain, extracted according to methods employed for Substance P, but devoid of ileum contracting properties, displayed comparable inhibitory effects upon the CNS. [See Abstract 1575]

[No address]

2498 LaDou, Joseph, Ellman, George L., Hallaway, Enoch, III, Edminster, Ivan F., Christensen, Robert L. Correlates of manifest anxiety. *Journal of Psychosomatic Research*, 1962, 6, 41-47.

Hippuric acid index and arm lift after-contraction with clinically rated manifest anxiety and psychological tests (vocabulary list of the WAIS, a questionnaire similar to the MMPI, the Gottschaldt test and the troop word and color tests) were studied with 49 subjects. Some of the subjects were anxiety patients, and the controls were American Quentin prisoners, relatively anxiety free. The Ellman et al. technique modified by Kern et al. was used in the fluorometric determination of hippuric acid. The hippuric acid index correlated significantly with clinically manifest anxiety, but the amounts of hippuric acid excreted did not. The use of the index to establish values for expected excretions demonstrated the physical equality of high and low anxious groups. The after contraction predominated in subjects with low anxiety and demonstrated a high correlation with hippuric acid indices. Psychological tests correlated highly with clinical ratings of anxiety, but not with the index and after-contraction.

Department of Psychiatry
University of California
San Francisco, Calif.

2499 Shinfuku, Naotake, Sarai, Keisuke, & Ujihara, Heihachi. Excretion of the total and the unconjugated 17-hydroxycorticosteroids in schizophrenics. *Yonago Acta Medica*, 1962, 6, 16-21.

The excretion of total and unconjugated 17-OHCS by 15 schizophrenics, was assayed in 24-hour urine samples for 3 successive days. The excretion of total 17-OHCS tended to be low and unconjugated 17-OHCS high in patients, especially so in long hospitalized and inactive patients. Samples were taken before and after ECT in 13 cases; results varied, but total corticosteroids showed increased excretion in most cases related to good therapeutic effects. The unconjugated 17-OHCS tended to decrease after ECT. Altered excretion of unconjugated 17-OHCS often observed in schizophrenics or after

ECT seems to reflect a change in the metabolic condition of the liver.

Department of Neuropsychiatry
Tottori University School of Medicine
Tottori, Japan

2500 Culley, W.J., Saunders, R.N., Mertz, E.T., & Jolly, D.H. Effect of phenylalanine and its metabolites on the brain serotonin level of the rat. *Proceedings of the Society for Experimental Biology and Medicine*, 1962, 111, 444-446.

Wistar rats were placed on diets supplemented with 7% phenylalanine, 4.5% phenylpyruvic acid, 3% 5-hydroxyphenylacetic acid or 4% phenylacetic acid. Chromatographic analysis of brain samples revealed that serotonin levels were depressed most effectively by supplementing the diet with 7% phenylalanine. Phenylpyruvic acid diminished brain serotonin levels less effectively, while phenylacetic acid and o-hydroxyphenylacetic acid did not produce significant alterations in brain serotonin levels.

Mental Retardation Research Laboratory
Muscatatuck State School
Butlerville, Ind.

2501 Batrinos, M.L., De Verbizier, J., Moncuit, M., & Courjaret, J. L'excrétion de la FSH au cours du traitement par la lévomepromazine. [Excretion of FSH during levomepromazine treatment.] *Revue Française Etudes Clinique et Biologique*, 1961, 7, 521-523.

Urinary excretion of FSH was assayed in 6 physically normal women, aged 28-39 years. These psychiatric patients were receiving 300 mg levomepromazine p.o. daily. Assay was made before treatment and repeated from the 10th to the 30th day, and then was continued from the 31st to the 90th day of treatment. Assay was made through injecting an alcohol precipitate of urine into 18 day old mice and noting the increase in uterine volume (Batrinos 1959); normal values are 5-25 mouse units. No systematic alteration in FSH was noted. Apparently levomepromazine does not disturb the

genital cycle.

Hôpital Broussais
Paris, France

2502 Itoh, Tadao, Matsuoka, Masami, Nakazima, Kazuhiko, Tagawa, Kunio, & Imazumi, Reiji. An isolation method of catecholamine and effect of reserpine on the enzyme systems related to the formation and inactivation of catecholamines in brain. *Japanese Journal of Pharmacology*, 1962, 12, 130-136.

DOPA, dopamine and levarterenol in guinea pig brains can be easily separated by Duolite C-25 resin column chromatography and measured fluorometrically. The animal received 15 mg/kg reserpine i.p. Additionally Glenner's (1957) histochemical methods were used on brain slices, demonstrating an activating effect on MAO by reserpine in all brain areas, especially the hypothalamus. Dopamine and levarterenol were proven to be synthesized from DOPA by brain homogenates in vitro. The activities of DOPA carboxylase and dopamine β -oxydase were increased by reserpine administration, as is true of MAO activity. Increased enzymic activity related to the formation and activation of catecholamines, caused by reserpine administration, resulted in an increase in total acid catechols in the brain.

Department of Pharmacology
Osaka University Medical School
Osaka, Japan

2503 Speck, Louise B. Effects of massive X-irradiation on rat electroencephalograms and brain serotonin. *Journal of Neurochemistry*, 1962, 9, 573-574.

EEG's of unanesthetized Sprague-Dawley rats were made with implanted phonograph needle electrodes before and after X-irradiation. Whole body irradiation was delivered at 98.4 r/minutes for 4500, 9000 or 20000 r. Decreased 5HT (serotonin) levels were found immediately after exposure to 9000 r and 18 hours after 4500 r, coinciding with EEG slowing and lethargy. Later 5HT levels returned to normal even

though some animals showed severe delayed radiation sickness.

Department of Physical Medicine and Rehabilitation
University of Colorado Medical Center
Denver, Colo.

2504 Van Pilsum, John F., & Halberg Franz. A method for the determination of argininosuccinic acid in human urine. *American Journal of Mental Deficiency*, 1962, 67, 82-89.

A newly developed laboratory test designed to detect argininosuccinic acid in human urine is predicated on the assumption that only creatinine and argininosuccinic acid react with orthonitrobenzaldehyde to yield products which give a positive Sakaguchi color reaction. An 88% "recovery" of argininosuccinic acid intentionally added to human urine was obtained by this procedure. A total of 192 mentally retarded individuals was screened for argininosuccinic acid excretion, and amounts of argininosuccinic acid in excess of 300-500 mg/day were not detected in any of the urine samples. The technique here described is efficacious as a screening procedure in large scale investigations of the mentally retarded.

Department of Physiological Chemistry
University of Minnesota Medical School
Minneapolis 14, Minn.

2505 Kirberger, Ernst. Differentialdiagnostische Überlegungen bei vermehrter 5-Hydroxyindoleessigsäure-Ausscheidung im Harn. [Differential-diagnostic considerations in cases of increased urinary 5-hydroxyindoleacetic acid excretion.] *Deutsches Medizinische Wochenschrift*, 1962, 87, 929-934.

A patient excreted up to 100 mg 5HIAA daily; this was traced to eating walnuts. Walnuts were subsequently found to contain 17-34 mg% 5HT. This content is 10-50 times as high as that of other serotonin-containing fruits or food stuffs. The effect of food intake on urinary 5HT is reviewed. Excretion of more than 25 mg of endogenous 5HIAA can be considered pathognomonic for

ercinoid.

ervenklinik der Stadt
Frankfurt/Main, Germany

06 de Kalbermatten, J.P. Effet de la
rotonine sur l'hypersensibilité de dé-
rvation du ganglion sympathique cervical
olé du rat. [Effect of serotonin on the
ervation hypersensitivity of the isolated
mpathetic cervical ganglion in rats.]
elvetica Physiologica Acta, 1962, 20, 294-
5.

modified Larrabee technique was used
remove the superior cervical sympathetic
nglion from rats with preganglionic and
stganglionic nerves attached. The materi-
was placed in buffer solution and con-
ected to 2 electrodes. The postganglionic
erve action potential increases in response
preganglionic supramaximal stimulation
ring 8-12 hours following excision of
e ganglion, probably due to a denervation
persensitivity induced by acetylcholine.
roniazid (100 µg/ml) was added 4, 6
nd 22 hours after excision. The response
supramaximal stimulation was measured.
roniazid inhibited synaptic transmission
the superior cervical sympathetic gang-
on. The greater the lapse of time before
roniazid addition, the greater the inhibi-
on. At equimolar concentrations nialamide
nd pivalylbenzhydrazine display the same
hibiting action as iproniazid. In order to
etermine whether serotonin or levarter-
nol is the more important acetylcholine
ntagonist when MAO is inhibited, methy-
ergide and piperoxane, serotonin and
evarterenol inhibitors respectively, were
dded to the medium. Serotonin is the
ore important antagonist. The supersen-
itivity to acetylcholine in vitro immediately
fter denervation is probably due to a
ecrease in serotonin production or to
erotonin loss through membrane damage.

stitut de Pharmacologie
niversité de Lausanne
ausanne, Switzerland

507 Foldes, Francis F., Zsigmond, El-
ner K., Foldes, Veronika M., & Erdős,
Ervin G. The distribution of acetylcholin-

esterase and butyrylcholinesterase in the
human brain. *Journal of Neurochemistry*,
1962, 9, 559-572.

Acetylcholinesterase and butyrylcholines-
terase were examined in human brains
obtained at autopsy. The substrates were
acetylcholine (ACh), acetylthiocholine io-
dide, butyrylcholine iodide (BuCh), butyr-
ylthiocholine iodide and acetyl-β-methyl-
choline chloride (MeCh). Several inhibitors
including 1,5-bis (4-allyldimethyl ammoni-
um phenyl) pentane-3-1 dibromide and (2-
hydroxy-5-phenyl benzyl) trimethylam-
monium (bromide) dimethylcarbamate were
used. There were no marked differences
in the hydrolysis rates of acetylcholine,
butyrylcholine and acetyl-β-methylcholine
in the various cortical areas, as deter-
mined by respirometry and Koelle's (1955)
histochemical method. In the gray matter,
acetylcholinesterase (AChE) activity was
consistently higher than butyrylcholines-
terase (BuChE) activity. While AChE activ-
ity paralleled the total ChE activity, there
was relatively little variation found in
the BuChE activity of various areas. The
increasing order of AChE activity was:
cerebral cortex, cerebellar cortex, thala-
mus, globus pallidus and caudate nucleus.
No marked differences were found in the
AChE activity of the various areas of
the cerebral cortex. The AChE activity
of the white matter of the internal capsule
was higher, while that adjacent to the
cortical areas was lower, than that of the
cortical gray matter. BuChE activity in
the white matter was considerably higher
than in the gray matter. Hydrolysis activity
curves of ACh and MeCh by human gray
matter homogenates were similar to those
obtained for their hydrolysis by human
red cells. The BuCh hydrolysis activity
curve for white matter homogenates was
similar to that obtained in plasma. B.W.-
284C51 at 10 µM selectively inhibited the
AChE of both the human brain and red
cell. The inhibitory effect of 0.05 µM
RO2-0683 on the hydrolysis of BuCh by
human brain homogenates was less than
that on human plasma. With the histo-
chemical method, the specific staining caused
by AChE activity was primarily present
in a granular pattern in the protoplasm of
the neurons. The nuclei were free of specific
staining. The distribution of ChE activity

in the white matter was diffuse.

Department of Anesthesiology
Mercy Hospital
Pittsburgh, Pa.

2508 Håggendal, J. On the use of strong exchange resins for determinations of small amounts of catecholamines. *Scandinavian Journal of Clinical and Laboratory Investigations*, 1962, 14, 537-544.

Epinephrine and levarterenol can be separated from dopamine by being passed through a strong cation exchange column which tends to hold back their 3 o-methylated derivatives. Using Dowex 50 and Amberlite CG-120, complete separation of levarterenol, epinephrine, normethanephrine, metanephrine, and dopamine was possible in 1 run by eluting with HCl. Destruction of catecholamines can be controlled by means of antioxidant and chelating agents. Columns of thoroughly purified strong cation exchange resins were found to give off fluorescent material which can interfere with determinations.

Department of Pharmacology
University of Göteborg
Göteborg, Sweden

2509 Nukada, Tadaatsu, Matsuoka, Masami, & Imaizumi, Reiji. The effect of long-term administration of pyrogallol on the metabolism of catecholamines. *Japanese Journal of Pharmacology*, 1962, 12, 57-61.

Male rabbits were injected with 20 mg/kg pyrogallol/day s.c. for 5 weeks. Also male rats were given 50 mg/kg pyrogallol/day for 5 weeks, the observation period extending for 10 weeks. Column chromatography, modified after Nakajima (1960), was used for the determination of urinary catecholamines. The rate of excretion of o-methylated derivatives of catecholamines in the urine decreased briefly during the administration, but after longterm treatment with pyrogallol it returned to normal. Daily treatment with pyrogallol increased the rate of excretion of free catecholamines and the rate reached a maximum after 3 weeks. Longterm treatment with pyrogallol tends

to increase COMT and MAO activities in the liver. Enzyme activities related to the regulation of catecholamines are adaptively altered by changes in the endogenous catecholamine levels.

Department of Pharmacology
Osaka University Medical School
Osaka, Japan

2510 Put, T.R., & Meduski, J.W. The effect of adrenalectomy on the 5-hydroxytryptamine metabolism in the rat. *Acta Physiologica et Pharmacologica Neerlandica*, 1962, 11, 240-256.

The effect of acute bilateral adrenalectomy on 5HT metabolism was studied in rats using bioassay of brain 5HT and spectrophotometric determination of the urinary 5HIAA. The changes observed suggest a biphasic type of metabolic response. The 1st postoperative phase is characterized by an immediate increase in urinary 5HIAA, unchanged 5HT brain levels and impairment of the 5HT binding and storage mechanisms. A probable mechanism of 5HT binding and release is hypothesized. Clinically, in order to diminish prolonged postoperative parasympathomimetic responses, a careful pre-examination of the patient's adrenal status and tissue phosphorylation capacity should be performed. Any impairment indicates application of substitution therapy before the surgery.

Department of Neurosurgery
Neurological Clinic
University of Utrecht
Utrecht, The Netherlands

2511 Schiller, Mauricio Brandon. Efeito inibidor do cobre sobre o consumo de oxigênio pelo cérebro. [Inhibitory effect of copper on oxygen consumption by brain tissue.] *Jornal Brasileiro de Psiquiatria*, 1962, 11, 45-49.

Brain homogenates from male rats were prepared and run manometrically in 0.1 M, pH 7.4 buffer and various concentrations of copper. A concentration of 1.0 μ g per ml slightly inhibited oxidation and 1.3 μ g/ml markedly inhibited it.

Clínica Psiquiatria
Faculdade Nacional de Medicina
Universidade do Brasil
Rio de Janeiro, Brazil

2512 Constantinidis, J., Taban, Ch. H.,
Garrone, G. Examens biologiques dans
les syndromes mélancoliques. [Biological
tests in melancholic syndromes.] Praxis,
1962, 51, 590-596.

Various metabolic modifications exist in
melancholia and the most fruitful means
of research is through the investigation
of monoamines. Four categories of melan-
cholia were studied: manic-depressive
reaction, depressive type; recurring melan-
cholia; Cotard's syndrome; and, melan-
cholia with complications. Age increased
in relation to these 4 groups: 48 years
of age in the 1st, 55 in the 2nd, 72 in the
3rd and 73 in the 4th. Urinary steroid
excretion was low in these patients, particu-
larly in Cotard's syndrome. The Thorn
test for ACTH however showed normally
reactive adrenal glands. On examination of
serum proteins, fraction α_1 was low at
all ages and the γ -globulin was also low
particularly in cases with somatic com-
plications. Cholesterol was only increased
in the aged. Euglobulins were not modified
in the young, but were in the aged. 5HIAA
excretion levels appeared higher than nor-
mal in depressive syndromes and typical
melancholia, with higher levels in the older
patients.

Clínique psychiatrique universitaire
de Bel-Air
Geneva, Switzerland

2513 Kuno, M., & Muneoka, A. Further
studies on site of action of systemic omega-
amino acids in the spinal cord. Japanese
Journal of Physiology, 1962, 12, 397-409.

The action of a series of omega-amino
acids injected i.v. into cat spinal cord
was determined by means of intracellular
recordings and monosynaptic reflex testing.
The action of 7 and 8 carbon acids opposed
that of the shorter chain acids, facilitating
extensor monosynaptic reflexes and de-
creasing flexor reflexes. Action of the

longer chain acids resembled that of the
shorter chain acids in the following re-
spects: effects on spinal reflexes were
absent in decerebrate cats and present
in spinal preparations; the effect on flexor
monosynaptic responses was reduced fol-
lowing strychnine administration, and the
effect on flexor monosynaptic responses
was abolished by conditioning volleys of
high threshold afferent fibers from ex-
tensor muscles. GABA produced depression
of extensor motoneurons with increased
membrane potential and facilitation of flex-
or motoneurons with decreased membrane
potential. A long chain omega-amino acid
depolarized extensor motoneurons and hy-
perpolarized flexor motoneurons. Some
polysynaptic potentials were changed by
GABA injection without appreciably chang-
ing monosynaptic spike potential and in-
hibitory postsynaptic potentials from the
antagonistic muscle afferent fibers. Some
interneurons were depressed and others
were facilitated by GABA. Significant ef-
fects of GABA were not found in Renshaw
cells. Apparently, short chain omega-amino
acids selectively depress certain spinal
interneurons, while longer acids activate
these same interneurons.

Department of Pharmacology and
Physiology
Yamaguchi Medical College
Ube City, Japan

2514 Miyake, Hiroshi, Miyazaki, Masa-
toshi, & Imaizumi, Reiji. Determination of
urinary 3,4-dihydroxymandelic acid (DOMA).
Japanese Journal of Pharmacology, 1962,
12, 163-165.

A method for the determination of urinary
3,4-dihydroxymandelic acid (DOMA) is de-
scribed based on alumina adsorption, frac-
tionation with anion exchange resin and
extraction coupled with a conversion re-
action of DOMA to protocatechu aldehyde
followed by development and optical read-
ing at 495 m μ as well as paper chromato-
graphy. By this method 10 rabbits were
examined in related to 24-hour DOMA
excretion; the mean was ca. 720 μ g/50 mg
creatinine. Under the same conditions
levarterenol, insulin, reserpine, iproniazid,
pyrogallol and acetylcholine were adminis-

tered s.c. Respective increases in DOMA excretion after these drugs was 74, 168, 66, 38, 37 and 144%. The effect of electrical stimulation of rabbit hypothalamus was also studied; before stimulation DOMA μg per 50 mg creatinine was 10.4, while after stimulation 31.3 and blood glucose before and after figures were 88 and 110 mg%. Results are parallel to those for VMA excretion (Miyaki 1961). A substantial portion of endogenous epinephrine and of levarterenol may undergo oxidative deamination as the 1st metabolic step. Assay of DOMA represents another approach to inquiry on endogenous levels of epinephrine and levarterenol.

Department of Pharmacology
Osaka University Medical School
Osaka, Japan

2515 Miyake, Hiroshi, Yoshida, Hiroshi, & Imaizumi, Reiji. Determination methods for urinary 3-methoxy-4-hydroxymandelic acid and 3,4-dihydroxymandelic acid. Japanese Journal of Pharmacology, 1962, 12, 79-92.

The method of Sandler and Ruthven (1959) was modified for the determination of urinary vanilmandelic acid (VMA; 3-methoxy-4-hydroxymandelic acid) and 3,4-dihydroxymandelic acid (DOMA). The 3 additions to the original method were: the use of a Dowex, 1 x 2 (0.5 x 10.0), 2 step dilution and the use of a buffer blank. Urine samples were studied from normal male and female subjects, diurnal and nocturnal periods, and before and after a delivery. VMA did not exist in sulfate and glucuronide conjugates. VMA excretion values for 20 normal adults were: daytime ca. 9.9 μg DOMA/10 mg creatinine, while at night the corresponding value was about 4.2 μg . The pattern at parturition was characterized by a very high peak found in the 30 minute urine sample taken 150-180 minutes after delivery. In rabbits, DOMA values more than doubled after s.c. administration of either insulin or levarterenol.

Department of Pharmacology
Osaka University Medical School
Osaka, Japan

2516 Seferian, V. Sérotonine et cholérèse [Serotonin and choleresis.] *Thérapie*, 1962, 17, 185-187.

Bile was collected from dogs for 120 minutes before and after 5HT injection and volumes calculated 15 minutes before and after injection. The average dose of 5HT administered i.v. was 2.16 mg/kg. 5HT did not have a choleric effect; in fact bile flow diminished temporarily.

Faculté Française de Médecine
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Beyrouth, Lebanon

2517 Brochmann-Hanssen, E., & Svendsen, A. Baerheim. Gas chromatography of alkaloids, alkaloidal salts, and derivatives. *Journal of Pharmaceutical Sciences* 1962, 51, 1095-1098.

A gas chromatography machine equipped with an argon β -ionization detector and columns of silicone rubber SE 30 was used in the analysis of 69 alkaloids, alkaloidal salts and derivatives. The list included atropine, caffeine, cocaine, codeine, morphine, nalorphine, opiates, scopolamine and strychnine. The method was also applied to extracts of crude drugs. Phenolic alkaloids are readily gas chromatographed as the trimethylsilyl ethers. Alkaloidal salts were chromatographed directly. The salt dissociates in the flash heater and the alkaloid is eluted as the base. Under certain conditions many alkaloids decompose when subjected to gas chromatography. These decompositions often appear to be catalyzed by the glass wool used on top of the column packing.

University of California School of Pharmacology
Medical Center
San Francisco, Calif.

2518 Sivadon, M.P., Rouquette, J., & Souris, M.M. Recherche sur le pouvoir histaminopexic du sérum dans les affections mentales. [Investigation of the histaminopexic properties of serum from mentally disturbed persons.] *Annales Médico-Psychologiques*, 1962, 120, 1, 832-837; discussion 837-839.

The histaminopexic potential of sera was determined in 75 neurotic and psychotic patients on isolated guinea pig ileum. Nearly 1/3rd of the patients (15 neurotics, 9 psychotics) had a histamine-fixing power (PHP) of 0, 14 others a PHP of 5%, 24 a PHP of 10%, 11 a PHP of 15-20%, and only 1 a PHP of 25 and 30% respectively. There seems to be some direct connection between allergy and mental disturbance.

Centre Psychiatrique du Château
La Verrière, France

2519 DeMoor, P., Hinnekens, M., Steeno, O., Deckx, R., Delaere, K., & Meulepas, E. Corticosteroid metabolism during the combined administration of ACTH and catecholamines. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 138-149.

In normal men (94) and women (51), amounts of epinephrine and levarterenol (7.5-120 mg/kg) were added to infusions of 40 i.u. ACTH given i.v. over 8 hours in 500 ml of saline. Results of combined administration of ACTH with catecholamines were compared to those obtained with ACTH alone (in 42 men and 42 women). In men 2 effects were observed: a significant decrease of plasma corticosteroid concentration during and at the end of infusion when small amounts of catecholamines were added to ACTH and a significant increase of plasma corticosteroid concentration with doses at least 5 times larger of catecholamines. Using the analog computer analysis it could be shown that these effects were due to a constant removal rate r when more than 25 mg per minute per kg of catecholamines was added to the ACTH infusion and an increase in production rate p probably due to a contraction of the readily miscible pool when large doses (120 mg/minute/kg) were administered. In women no effect on removal rate, but only the increase in p factor was found. The increase in free corticosteroid removal rate observed in men is not due to an accelerated A-ring hydrogenation and conjugation of the corticosteroids or to an additional storage of corticosteroids in the red blood cells. Sex difference noted during the combined administration might explain certain of the sex differences in stress-

induced pathology.

Laboratorium voor Experimentele
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Rega Instituut
Universitaire Klinieken St. Rafaël
Louvain, Belgium

2520 Smith, Elizabeth R.B., & Weil-Malherbe, H. Metanephrine and normetanephrine in human urine: method and results. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 212-223.

The amount of metanephrine and normetanephrine excreted were assayed through: hydrolysis of urine at pH 1, passage through an alumina column, electrodialytic desalting, incubation with sulfatase and adsorption of amines on a cation exchange resin. The final eluate of the 2 amines was estimated fluorometrically on the principle of the trihydroxyindole methods. Methanephrine is oxidized at pH 3 and both amines are oxidized in a separate aliquot at pH 8. This method is able to estimate 0.02 μ g metanephrine and 0.2 μ g normetanephrine per sample. The mean 24-hour excretion of metanephrine was 80 μ g and that of normetanephrine about 160 μ g. Although 4-hour excretion rates showed definite diurnal variations in some individuals, these variations were not consistent and their mean values, with 1 exception, did not significantly deviate from the excretion rate calculated for the entire 24-hour period. Variations in metanephrine and normetanephrine excretion during successive 4-hour periods showed a highly significant correlation.

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2521 Jérôme, Henri. Anomalies du métabolisme du tryptophane dans la maladie mongolienne. [Anomalies of tryptophan metabolism in mongolism.] *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, 1962, 113, 168-172.

Determination of the α -amine nitrogen (Sørensen method) and total nitrogen (Kjeldahl method) on 31 mongolian and 21 control children showed no differences in the 24-hour urine determinations of total nitrogen, while the α nitrogen was significantly different in the mongolian children. The levels of α -amine nitrogen and total nonprotein nitrogen in the blood are higher in mongolians. The difference was, however, not statistically significant. Mongolian children excrete less 5HIAA, 3 indole acetic acid (IAA) and xanthurenic acid, while the cy-nurenine excretion is the same. The catabolism of 5HT to 5HIAA seems to be normal in mongolian children. The deficit in 5HIAA, IAA, xanthurenic acid elimination in these children may be due to 1 of 2 causes: a higher renal threshold, or loss of equilibrium of the intermediate metabolism.

Institut de Progenèse
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Paris 6°, France

2522 McLennan, H. Some effects of the catecholamines on spinal cord reflexes. *Journal of Neuropsychiatry*, 1962, 4, 125-126.

Since systemic administration of epinephrine inhibits spinal reflexes, further work was done to determine the effects of topically and systemically administered catecholamines (epinephrine, levarterenol, and dopamine) on the spinal cord. Brain extracts and dopamine shared a similarity of action. Dopamine might bear some resemblance to the transmitter substance active at inhibitory synapses; effects are differently engendered than those which follow topical application when produced after systemic catecholamine administration. Stimulation of points in the bulbar reticular formation inhibit spinal reflexes. This inhibition may be blocked by dichloroisoproterenol (DCI) and strychnine but is unaffected by dibenzylamine or chlorpromazine. In an attempt to localize the site of

catecholamine action, DCI was administered to determine its effect upon the direct inhibitory pathway exerted upon antagonistic motoneurons by stimulation of the Ia afferent fibers from a protagonist muscle. The extent of the inhibition produced in this pathway was unaffected by a dose of DCI which markedly reduced the inhibition resulting from stimulation of the reticular formation. Therefore, dopamine does not act at the inhibitory synapses in these systems, at least not at the final synapse of the motoneuron.

Department of Physiology
University of British Columbia
Vancouver, Canada

2523 Pluvinage, R., & Lelus, R. Alcoolisme chronique et carence en pyridoxine [Chronic alcoholism and pyridoxine deficiency.] *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, 1962, 113, 1030-1036.

Vitamin B₆ deficiency was measured by establishing normal xanthenuria after tryptophan administration, and then measuring the level in alcoholics. Of 113 cases, negative or doubtful results were obtained in 48, and moderate to high results were registered in 65. Pyridoxine deficiency was thus definitely demonstrated in about 58% of the cases, or 85% on the basis of further tests with tryptophan surcharge. There is no relationship between xanthenuria rates and the severity of clinical symptoms. Xanthenuria can not be correlated with the levels of blood protein, the total cholesterol or the esterification ratio; classical liver balance tests do not generally indicate the severity of psychological and digestive troubles.

Service de Neurologie
Hospice de Bicêtre
Paris, France

2524 Lehmann, J., & Karamustafaoğlu. Rapid differentiation of barbiturates in blood serum by thin-layer chromatography. *Scandinavian Journal of Clinical and Laboratory Investigation*, 1962, 14, 554-558.

1-dimensional thin-layer chromatograph-method for the differentiation of barbiturates in serum which can be run in 1-1.5 hours is presented. For the differentiation of the barbiturates, 2 sets of standard solutions and the test sample are used. By spraying 1 set with permanganate the compounds with double bonds are indicated, and by spraying with carbazole and mercuric nitrate all barbiturates are visualized on the chromatogram which allows the differentiation of the barbiturates.

Central Laboratory for Clinical Chemistry
Södersjukhuset's Hospital
Stockholm, Sweden

25 Tursky, T., & Sajter, V. The influence of potassium cyanide poisoning on the γ -aminobutyric acid level in rat brain. *Journal of Neurochemistry*, 1962, 9, 519-523.

Cyanide intoxication of rats, mice and guinea pigs with KCN (40 mg/kg i.p.) decreased the brain GABA level to 68-75% of control concentration and simultaneously increased glutamic acid to 106-110%. This decrease is similar for both adults and juveniles. After intracerebral administration of U-C¹⁴ labeled glutamic acid a higher specific activity of glutamic acid and a lower of GABA was found in cyanide-intoxicated animals. Hypoxia in an atmosphere of nitrogen or carbon dioxide does not influence either GABA level or glutamic acid level. The decrease of GABA is caused by inhibition of glutamic decarboxylase.

Department of Biochemistry
Comenius University
Bratislava, Czechoslovakia

26 Boger, William P., & Gavin, John J. Phenylketonuria. I. Validation of microbiologic assay for serum l-phenylalanine. *Journal of Laboratory and Clinical Medicine*, 1962, 60, 695-699.

Serum l-phenylalanine may be estimated using *Leuconostoc mesenteroides* P 60 (TCC 8042) as the test organism. Values obtained are in good agreement with those obtained by the La Du and Michael (1960)

chemical method and conform to published figures. The method is simple, reliable, economical and adaptable to handling large numbers of samples.

[No address]

2527 Allgén, L.G., Izikowitz, S., Ordell, Inga-Britt, & Salum, Inna. Clinical biochemical studies in delirium tremens and other acute psychiatric sequels of alcohol abuse. I. Serum iron. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 40-51.

The serum iron level was studied in 123 male alcoholics with delirium tremens and in 211 male patients with allied conditions in acute and convalescent stages. During the acute stage the group mean values of serum iron were below normal in more serious conditions (delirium tremens). The lowest mean value in any patient was 15 μ g/100 ml. There was a steady decrease of group mean values (μ g/100 ml) from the milder conditions to the more severe ones. Syndrome B₁ ca. 142.9, syndrome B₂ ca. 136.3, syndrome C 114.6, DT₁ ca. 80.5, DT₂ ca. 60.6 and DT₃ ca. 51.6. In the milder conditions there was a high percentage of abnormally high values, the highest mean being 305 μ g/100 ml. In some cases a rapid decrease in the serum iron level was noted at an early stage. High serum iron values disappeared during convalescence. Among other causes, acute liver cell damage has been considered as possibly responsible for the hypersideremia and stress-induced changes in iron kinetics as possibly responsible for the hyposideremia.

Beckomberga Hospital
Bromma 4, Sweden

2528 Wallenius, Gunnar, Zaar, Bertil, & Lausing, Endel. A rapid method for determination of barbiturate in serum or urine. *Scandinavian Journal of Clinical and Laboratory Investigation*, 1962, 15, 252-256.

Serum (0.2 ml) or urine is soaked into an upper filter rod (CS 719 from Cigarette Components Limited, London) and 0.3 ml

of Hg reagent solution [acidified $\text{Hg}(\text{NO}_3)_2$] is pipetted into a lower filter rod; 0.3 ml dithizone solution is pipetted into a graduated test tube and the extraction column is fitted into the top of the tube. Chloroform is now slowly pipetted into the column on top of the sample-containing filter until a volume of 5 ml is drained down into the tube. Extraction takes about 1.5 minutes. Depending upon the amount and nature of the barbituric acid derivative, the color of the dithizone solution will turn from green to orange allowing spectrophotometric assay at 605 m μ .

Department of Clinical Chemistry
University Hospital
Uppsala, Sweden

2529 Brown, J.K., Malone, M.H., Stuntz, D.E., & Tyler, V.E. Paper chromatographic determination of muscarine in *Inocybe* species. *Journal of Pharmaceutical Sciences*, 1962, 51, 853-856.

A relatively simple paper chromatographic method was developed quantitatively to determine muscarine content in small dried samples of mushroom tissue in order to establish relative toxicity. This technique entailed duplicate spotting with suitable quantities (3-100 μl) of the purified extract on a buffered chromatogram. The chromatogram developed with Thies and Reuther's reagent to determine the minimum amount of extract which formed a detectable orange-red spot. Actual quantities applied varied according to the concentration of muscarine in the extract. If subsequent chromatograms verified initial observations, the quantity of extract producing a detectable muscarine spot was considered equivalent to 6 μg of muscarine. Concentrations of muscarine in dried carpophores were calculated from the resultant data. Application of the procedure to 34 species of *Inocybe* revealed detectable quantities of muscarine ranging from 0.01 to 0.80% in ca. 75%. No significant relationship was found between muscarine distribution and species differences.

College of Pharmacy
University of Washington
Seattle 5, Wash.

2530 Sacks, William. Phenylalanine metabolism in control subjects, mental patients and phenylketonurics. *Journal of Applied Physiology*, 1962, 17, 985-992.

After injection of 90 μc phenylalanine- C^{14} , tyrosine- C^{14} , 1-phenylalanine- C^{14} , 45 μc 1-phenylalanine- C^{14} or 1-tyrosine- C^{14} into control subjects, mental patients and phenylketonurics, blood samples were collected, and total CO_2 activities were determined by the liquid scintillation method in duplicate, and results agreed within 3%. Other assays included specific activities of whole blood amino acid carboxyl carbon, lactate carboxyl carbon and whole blood glucose activities. After injection of phenylalanine- C^{14} or 1-phenylalanine- C^{14} , C^{14}O_2 specific activities in whole blood were 1/10 to 1/3 as high as those after injection of tyrosine- C^{14} or 1-tyrosine- C^{14} in the normal subjects and chronic psychotic patients. In phenylalanine- C^{14} studies, tyrosine specific activities were 1/16 to 1/10 of corresponding phenylalanine specific activities. Injection of 1-phenylalanine- C^{14} into 2 phenylketonurics, a 3-year-old girl and a 54-year-old man, revealed that C^{14}O_2 activities in the child approximate those in other experiments, whereas the were lower in the adult. Maximal tyrosine specific activity was 1/6 the corresponding phenylalanine specific activity. Ratios of specific activities of maximal C^{14}O_2 to phenylalanine were similar in controls and phenylketonurics, suggesting that the catabolism of phenylalanine proceeds at the same rate in phenylketonuria. Results with 1-phenylalanine- C^{14} indicated that more than the carboxyl carbon contributed to hemic C^{14}O_2 .

Rockland State Hospital
Orangeburg, N.Y.

2531 Kataoka, Kiyoshi. Subcellular distribution of 5-hydroxytryptamine in the rabbit brain. *Japanese Journal of Physiology*, 1962, 12, 623-638.

Particulate 5HT of rabbit brain was found in the heavier granule, the so-called synaptic vesicle (Whittaker 1959), as well as in the microsome, showing rather weak

K^+ , Ca^{++} and Mg^{++} showed hardly any activity up to 200 mM. Reserpine caused loss of about 40% particulate 5HT in 4 hrs. 5HT was susceptible to MAO, undergoing almost complete destruction when incubated at 4°C. 5HT-containing granules showed hardly any uptakes of 5HT when it was added to the media at 4°C. In the microsomal fraction, a 5HT inactivating action was noted which disappeared after diluting the fraction and which is also inhibited by iproniazid, but not activated either as reported by Whittaker.

Department of Physiology
Oto University School of Medicine
Oto, Japan

32 Fürst, W. Untersuchungen über Kupferverbindungen der Barbitursäurederivate. Investigation of the copper compounds of barbituric acid derivatives.] Pharmazeutische Zentralhalle, 1962, 4, 189-194.

A method is presented for the quantitative determination of barbituric acid derivatives in various drugs, when these are in the form of pills or capsules, or tablets or suppositories. The method makes it possible to precipitate, in crystalline form, barbiturate, copper pyridine compound in Barb. $Cu(Py)_2$ form, from highly diluted solutions.

Institut für Pharmazie
Munich, Germany

33 McMurray, W.C., Mohyuddin, F., Essiter, R.J., Rathbun, J.C., Valentine, H., Koegler, S.J., & Zarfes, D.E. Citrulluria. A new aminoaciduria associated with mental retardation. Lancet, 1962, No. 3, 3.

A 18-month-old mentally retarded child excreted copious amounts of urinary citrulline as detected by ion-exchange chromatography. Further work has revealed that large quantities of citrulline have been detected in all samples of the patient's urine, though amounts varied from 0.48-2.15 g per day over a 10-day period. Citrulline metabolism will be explored in the parents (who are 1st cousins) to investigate the

possible genetic nature of the lesion.

Department of Biochemistry
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London, Ontario
Canada

2534 Langer, Ella. Present and projected testing for phenylketonuria. Journal of the Maine Medical Association, 1962, 53, 69-70.

The Division of Maternal and Child Health in Maine now conducts ferric chloride tests on infants and older children to screen for unsuspected phenylketonuria. Detection of a case is promptly followed by institution of a low phenylalanine diet to prevent mental deficiency. Of 3 cases detected early, 2 have manifested obvious I.Q. improvement. Eventually, it is hoped that hospital screening of newborns by the blood phenylalanine-agar diffusion tests will eventually replace the urine screening test in older children. Aspirin and some tranquilizers produce false positive results in the ferric chloride test.

Division of Maternal and Child Health and
Crippled Children's Services
Augusta, Me.

2535 Lyons, J. Robert. Inhibition of mitochondrial ATP-ase and ATP- P_i exchange activity with Tofranil. Aviation and Medical Acceleration Laboratory Report, 1962, 6206, 1-14.

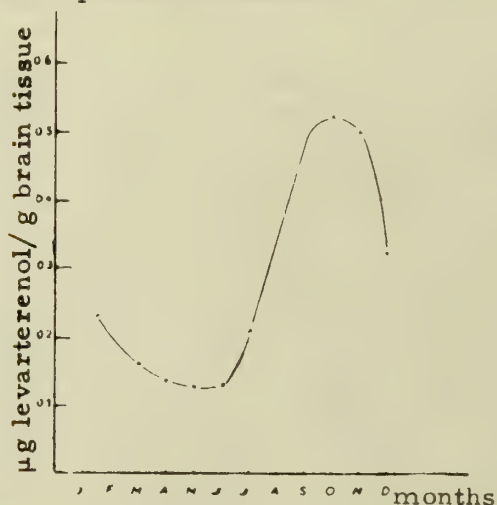
Using Warburg manometry, in concentrations of 10^{-4} M and higher, imipramine inhibited phosphorylation and O_2 uptake in mitochondria (rat liver). An almost complete block of O_2 uptake and phosphorylation was observed with 10^{-3} M imipramine. A decrease in P/O ratio was observed with increasing imipramine concentrations. A decrease in the amount of ATP split with increasing concentrations was also observed, i.e., 10^{-5} - 10^{-2} M imipramine. At 10^{-3} M imipramine caused ca. 50% inhibition of ATP-ase activity and the amount of ATP split approached 0 as the concentration of inhibitor increased. When the Mg/ATP molar ratio was kept constant at 0.13, imipramine was proven to cause noncom-

petitive inhibition of ATP-ase activity in mitochondria. Imipramine apparently competes with a site on the mitochondria which the substrate uses in order to participate in the reaction. Blocking ATP metabolism may prevent the cells from having an energy source available to maintain a normal potential difference across the membrane. If a presynaptic neuron did not release enough transmitter substance to cause the depolarization of the postsynaptic neuron, the postsynaptic neuron would not fire, but if the membrane potential of the postsynaptic neuron is lowered, then it may still be fired by a weaker transmitter. On the other hand the inhibitory in vitro effects described may have no bearing on drug action and merely represent toxicity.

Aviation and Medical Acceleration
Laboratory
Johnsville, Pa.

2536 Beauvallet, M., Fugazza, J., & Solier, M. Nouvelles recherches sur les variations saisonnières de la noradrénaline cérébrale. [New studies on seasonal variations in cerebral levarterenol (noradrenalin).] *Journal de Physiologie*, 1962, 54, 289-290.

Periodically, the brains were removed and extracted from adult Wistar rats kept under the same conditions and temperatures for a year. Assay was made fluorometrically. The peak was 0.52 $\mu\text{g/g}$ levarterenol in October, at the low 0.13 $\mu\text{g/g}$ in June. The curve is presented below.



Institut de Pharmacologie
Faculté de Médecine
Université de Paris

2537 Westerink, D. Chromatografische scheiding en microbepaling van fenobarbital, methylfenobarbital, butobarbital, fenytoïne. [Chromatographic separation and microdetermination of phenobarbital, methylphenobarbital, butobarbital and phenytoin.] *Pharmaceutisch Weekblad*, 1962, 24, 84-856.

Column partition chromatography on Celvol 545 was used for the separation of phenobarbital, methylphenobarbital, butobarbital and phenytoin. Amounts of 50-250 μg , determined by UV absorption spectrophotometry, gave reproducible results with recovery of 100-5%.

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Utrecht, The Netherlands

See also 2239, 2257, 2258, 2259, 2260, 2397, 2405, 2414, 2427, 2466, 2468, 2470

ABBREVIATIONS

-KG	α -ketoglutarate	HD	hypnotic dose
ACL	Zuckerman's Affect Adjective Check List	5HIAA	5-hydroxyindoleacetic acid
CTH	adrenocorticotrophic hormone	5HT	5-hydroxytryptamine
d lib.	free choice	5HTP	5-hydroxytryptophane
DP	adenosinediphosphate	i.a.	intraarterial
.M.	morning	ibid.	in the same place
MA	American Medical Association	i.e.	that is
rt.	Article	i.m.	intramuscular
TP	adenosinetriphosphate	IMPA	Lorr's Inpatient Multidimensional Psychiatric Scale
AL	British antiLewisite	i.p.	intraperitoneal
AS	benzyl analogue of serotonin	IPAT	Cattell's Institute for Personality & Ability Testing Anxiety Scale
i.d.	twice a day	I.Q.	intelligence quotient
OL	bromolysergic acid diethylamide	IU	international unit
UN	blood urea nitrogen	i.v.	intravenous
	Celsius scale	kg	kilogram
a.	about	K _i	Michaelis constant for an inhibitor
AR	conditioned avoidance response	K _m	Michaelis constant for a substrate
BS	chronic brain syndrome	lbs	pounds
c	cubic centimeter	LD	lethal dose
ED	convulsive dose	LSD	lysergide
m	centimeter		
m ²	square centimeter		
m ³	cubic centimeter		
C.N.R.S.	Centre National de la Recherche Scientifique	μ	micron
ENS	central nervous system	μ c	microcurie
COMT	catechol-o-methyl transferase	μ g	microgram
ps	counts per second	μ l	microliter
CR	conditioned reflex (response)	μ M	micromolar
S	conditioned stimulus	m μ	millimicrons
TD	Climbing Time Delay	M	molar
		ma.	milliamperes
		MACC	Motility Affect Cooperation Communication
DDT	dichlorodiphenyl trichloroethane	MAO	monoamine oxidase
OPA	3, 4-dihydroxy-phenylalnine	MAS	Taylor Manifest Anxiety Scale
PH	diphosphopyridine nucleotide	meq	milliequivalents
PNH	reduced diphosphopyridine- nucleotide	ml	milliliter
		mm	millimeter
CCG	electrocardiogram	mm ²	square millimeter
Ed.	editor	MMPI	Minnesota Multiphasic Person- ality Inventory
ED	effective dose	MSRP	Multidimensional Scale for Rating Psychiatric Patients
EDTA	ethylenediaminetetraacetic acid		
EG	electroencephalogram		
e.g.	for example		
ERG	electroretinogram	N	normal
et al.	and others	NEFA	nonesterified fatty acid
tc.	and so forth	NIMH	National Institute of Mental Health
	Fahrenheit scale		
FFA	free fatty acid	p	probability
	gram	PAH	para-aminohippuric acid
GABA	γ -aminobutyric acid	PBI	protein-bound iodine
GABOB	γ -amino- β -hydroxybutyric acid	pH	negative logarithm of the hydrogen ion concentration

P _i	inorganic phosphate	TAT	Thematic Apperception Test
P.M.	afternoon and evening	TH	thyroid hormone
p.o.	by mouth	t.i.d.	thrice a day
ppm	parts per million	TPN	triphosphopyridinenucleotide
PRP	Psychotic Reaction Profile	TPNH	reduced triphosphopyridine-nucleotide
q.i.d.	four times a day	TSH	thyroid-stimulating hormone
refs.	references	U	unit
R _f	ratio of the distance of dissolved substance to solvent distance	UR	unconditioned response
RNA	ribonucleic acid	US	unconditioned stimulus
ru	rat unit	USAF	United States Air Force
s.c.	subcutaneous	USDHEW	United States Department of Health, Education, and Welfare
S.D.	standard deviation	USP	United States Pharmacopoeia
SGOT	serum glutamic oxaloacetic transaminase	USPHS	United States Public Health Service
SGPT	serum glutamic pyruvic transaminase	UV	ultraviolet
sic	exactly as found	VA	Veterans Administration
SOSAI	Springfield Outpatient Symptom and Adjustment Index	viz.	namely
SRA	Science Research Associates	WAIS	Wechsler Adult Intelligence Scale
Suppl.	supplement	WPRS	Wechsler Psychiatric Rating Scale

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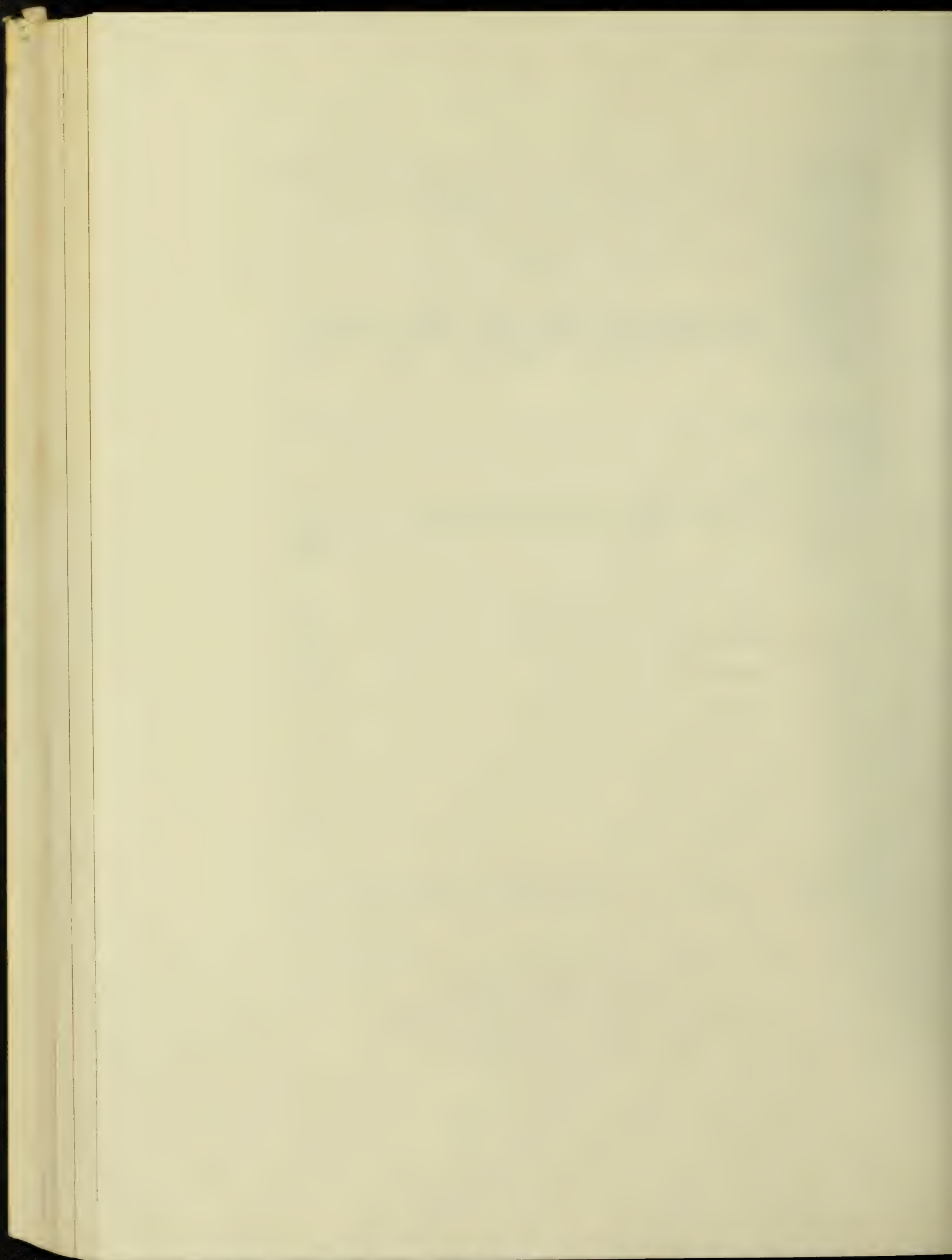
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Psychopharmacology Abstracts

Volume 2, Number 11

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REVIEWS, SUMMARIES, BIBLIOGRAPHIES,
AND GENERAL ARTICLES AND BOOKS

538 Schipa, Silvana. Recenti acquisizioni sugli steroidi ormonali e loro applicazione in neuropsichiatria ed anesthesiologia. [Recent acquisitions in hormonal steroids and their application in neuropsychiatry and anesthesiology.] *Folia Psychiatrica*, 1961, 1, 329-371.

The biogenesis of steroids, the functions of estrogens, androgens and corticoadrenal hormones, classifications, biological activity metabolism and urinary excretion, as well as their application in rheumatology, neuropsychiatry and anesthesiology are described. Optimal results have been obtained in the field of rheumatology. In the field of psychiatry, steroids have not markedly improved the prognosis of severely disturbed patients. In neurology their application is restricted to chorea minor, polyneuritis, etc., and in anesthesiology steroids have found wide application. (281 refs.)

Ospedale Psichiatrico Interprovinciale
Salentino
G. Libertine
Lecce, Italy

539 Lorrain, André. Les médications psychotoniques modernes. [Modern psychotonic drugs.] *Lille Médical*, 1961, 6, 1001-1007.

Psychotonics, in the strict sense, are used in asthenia, e.g., after operations, alcoholic bouts; as antagonists to barbiturates, e.g., to control drowsiness in barbiturate treated epileptics; to control akinesia in parkinsonism and drug-induced extrapyramidal reactions, and finally, in the treatment of narcolepsy. The 1st drugs used were the amphetamines. Piperadol, methamphetamine, levophaceterane, morphine, amphetamine, phenmetrazine, imipramine, nialamid, centrophenoxyne and other agents are noted. (No refs.)

No address]

540 Gayral, L. Les nouveaux sédatifs nerveux: "tranquillisants" et neuroleptiques. A effect tranquillisant. [New nervous sedatives: tranquilizers and neuro-

leptics; the tranquilizing effect.] *Concours Médical*, 1961, 83, 6761-6762; 6764.

Nervous sedatives or tranquilizers are drugs directed against anxiety from multiple causes. Among the older drugs, barbiturates still have their indications. Among the newer neuroleptics in wide application are: hydroxyzine, glutethimide, meprobamate, chlordiazepoxide, thioridazine, levomepromazine and benactyzine. Some of these are used in high dosages in the treatment of psychoses. (No refs.)

Clinique Neuropsychiatrique
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2541 Chih-fan, Ch'eng, & Ch'i-shan, Chang. Some early records of nervous and mental diseases in traditional Chinese medicine. *Chinese Medical Journal*, 1962, 81, 55-59.

The history of nervous and mental disease in the Chinese classics and medical literature from ancient times through the Ming and Ch'ing Dynasties (1368-1911) is briefly reviewed. During the T'ang dynasty various attempts were made to classify these aberrations. The major contribution to the study of these diseases was made by Wang K'en-t'ang of the Ming Dynasty who explicitly categorized insanity as composed of schizophrenia, mania and seizures. In the 11th century nervous and mental diseases were differentiated from organic diseases. Various treatments used in addiction and acupuncture included: *Epedra sinica*, *Siler divar icatum*, almond, *Atractylis ovata* and gypsum in the 7th century and drugs derived from mercury, musk and ox bezoar, introduced in the 12th century. (10 refs.)

Department of Medical History
Peking Medical College
Peking, China

2542 Batrinos, M.L., & DeVerbizier, J. L'action de la chlorpromazine sur le système endocrinien. [Action of chlorpromazine on the endocrine system.] *Revue Française d'Etudes Cliniques et Biolo-*

giques, 1962, 7, 87-97.

Clinically chlorpromazine may produce galactorrhea and disturbances in the menstrual cycle, usually amenorrhea. ACTH secretion in response to stress is suppressed; however the daily output of adrenal hormones does not seem to be affected, nor are thyroid hormone plasma levels. Its action is predominantly central, affecting the supraepiphyseal regional inhibiting centers which control pituitary secretion; there is also some direct effect on other endocrine glands. Simultaneous effect on different areas makes the evaluation of action difficult. In laboratory animals chlorpromazine at high doses has the following actions: a/ transitory stimulation of ACTH secretion; a partial depression of ACTH release in response to stress; no effect on exogenous ACTH, b/ disturbance of the sexual cycle tropins, c/ induction of mammary gland development and stimulation of secretion, d/ inhibition of TH secretion and direct depression of thyroid uptake of radioactive iodine, e/ increase of water retention following hydration both by stimulating ADH production and by facilitating its peripheral action, f/ neutralization or reversal of the hypertensive action of epinephrine without hindering other actions (the hypertensive action of levarterenol is also neutralized) and g/ hyperglycemic effects. (149 refs.)

Hôpital Broussais
Paris, France

2543 Stevenin, L. Les rapports de la psychothérapie et de la psychopharmacologie au Congrès de psychothérapie de Vienne (août 1961). [Reports on psychotherapy and psychopharmacology at the Vienna Psychotherapy Congress, August, 1961.] *Annales Médico-Psychologiques*, 1962, 120, 1, 849.

The association of psychotherapy with drug treatments in psychoses diminishes the number of relapses, and frequently in neuroses drugs are indispensable for the reduction of anxiety. The integration of psychotherapy with medical and pharmacological treatments was promulgated by a number of speakers. The author and Benoit suggested 3 therapeutic means of approach; narcoanalysis, weck analysis and dream analysis

corresponding to the use of 3 types of psychoactive agents; psycholeptics, psychoanalitics and psychodysleptics. At the Congress particular interest was shown in the last mentioned group of drugs in relation to psychotherapy. (No refs.)

[No address]

2544 Baruk, H., Launay, J., & Maurey G. Psychotoniques et épileptogènes. Note préliminaire sur le 2145 T.H. [Psychotonic and epileptogenics. Preliminary note on TH 2145.] *Annales Médico-Psychologiques*, 1962, 120, 1, 144.

Acetazolamide, (TH 2145), at moderate doses in monkeys has psychotonic action increasing initiative, exaggerating mimicking, making the animal lively and expressive. At high doses the drug causes negativism and autism. In clinical medicine, the stimulating effect is equally apparent. The problem of the relationship between psychotonics and epileptogenic action at high doses is reviewed. (No refs.)

[No address]

2545 Broggi, Frank S. Modified electrotherapy versus anti-depressant drugs. *Journal of the Maine Medical Association*, 1962, 53, 219-222.

The deleterious effects of unmodified ECT have precipitated its obsolescence. It encompasses numerous unwarranted and unnecessary hazards. Modified ECT remains the most reliable form of treatment, especially in severe psychotic depression. Definitive steps should be taken by the Maine medical profession to diminish the excessively high state suicide rate. Untoward effects from antidepressants like iproniazid, pheniprazine, isocarboxazid, phenelzine, amitriptyline and imipramine may be far more debilitating than any complication experienced with modified ECT. Unlike the antidepressants, liver, renal or cardiac impairment does not contraindicate utilization of modified ECT. (No refs.)

Portland City Hospital
Portland, Me.

46 Liberman, Robert, An analysis of the placebo phenomenon. *Journal of Chronic Diseases*, 1962, 15, 761-783.

any alteration in patient response resulting from therapeutic intent rather than physicochemical aspects of a medical procedure may be termed a placebo effect. The placebo phenomenon stems from 4 factors: the doctor-patient therapeutic situation which compasses the attitudes and behavior of the doctor, the physical environment and type of treatment; patient predispositions toward doctors and medicines, self-esteem and need for social approval, authoritarian and dependency tendencies and anticipatory anxiety; internal mediating processes of attention, comprehension, evaluation and acceptance which interact with the therapeutic stimuli and predispositions to produce the observed placebo effect. (No refs.)

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San Francisco, Calif.

47 Dorfman, Wilfred. The recognition and management of depression. *Journal of the Maine Medical Association*, 1962, 53, 257-259.

Various types of depression per se and depressive aspects of organic illness may be treated by psychotherapy, ECT and drug therapy (amphetamine, methylphenidate, nipramine and amitriptyline). Frequently, antidepressants may act synergistically with psychotherapy for optimal amelioration. (1 ref.)

Maine Medical Association
Portland, Me.

48 Grümer, Hanns-Dieter. Synopsis of some current studies in phenylketonuria. *Journal of the Maine Medical Association*, 1962, 53, 8-15.

Clinically, phenylketonurics are mentally retarded, exude a musty odor, exhibit neurological changes with hyperactivity and excrete phenylpyruvic acid copiously. Numerous biochemical studies finally elucidated the metabolic aberrations responsible for

phenylketonuria. Phenylketonuria has been induced in rats and mice. A phenylalanine-free diet initiated immediately after birth will frequently obviate development of mental retardation. Optimal results accrue from maintenance of the diet for a sustained period of time, even for life. (64 refs.)

Biochemical Laboratory
Pineland Hospital and Training Center
Pownal, Me.

2549 Eyres, Alfred E. Observations on psychiatry in certain areas of the Orient and the Middle East. *Journal of Neuropsychiatry*, 1962, 3, 171-176.

A description is given of the psychiatric facilities observed in a 6 week trip taken by the Eastern Psychiatric Research Association. Fifteen member psychiatrists visited Japan, Hong Kong, Thailand, India and Israel. In Japan, ECT has frequently been replaced by drug therapy. Methamphetamine addiction is a serious problem in Japan, while Thailand has numerous opium addicts. Thailand boasts treatment regimens for the mentally ill which include psychotherapy, pharmacotherapy and ECT. Psychiatric facilities are abysmal in India, with ECT constituting the mainstay for treatment. Israel enjoys good medical facilities, with ECT, insulin shock therapy and pharmacotherapy readily available for good psychiatric care. (No refs.)

Eastland Center Professional Building
17800 East Eight Mile Road
Detroit 36, Mich.

2550 Denber H.C.B., & Rajotte, P. Brèves considérations méthodologiques sur l'évaluation clinique des médicaments psychotropes. [Brief methodologic considerations on the clinical evaluation of psychoactive drugs.] *Comptes Rendus du Congrès des Médecins Aliénistes et Neurologistes (Montpellier, 10-15 July, 1961)*, 1962, 370-373; discussion 374. Montpellier: A. Coueslant.

Among the various parameters which must be taken into account in the evaluation of psychoactive drugs are the population of the patients, hospital conditions and the

personality of the investigator. The use of objective techniques such as double-blind, crossover, etc. are of aid in obtaining better comparisons. Emphasis is placed on the evaluation of haloperidol, butyrylperazine and chlorprothixene. In the discussion Fouks noted that chemotherapy allows contact with the patient and thereby increases the chances of psychosocial therapies. (13 refs.)

[No address]

2551 Heymans, C. Considérations sur l'interprétation des effets de l'électrochoc chez l'organisme réserpiné. [Considerations on the interpretation of electroshock effects in the reserpinized body.] Bulletin de l'Académie Royale de Médecine de Belgique, 1962, 2, 142-146.

The importance of peripheral catecholamine depletion caused by reserpine, without exclusion of the possibility of central action by the alkaloid, in relation to its utility in ECT, is reviewed. ECT causes hypertension in the normal animal through excitation of the vasoconstrictor centers. In the reserpinized animal, excitation of vasoconstrictor centers cannot act on the peripheral vessels because reserpine has depleted catecholamines at this level and thereby blocks peripheral vasoconstrictive adrenergic transmission. Marked prolonged apnea following ECT in the reserpinized animal is essentially due to the marked and prolonged reserpinized-induced drop in blood pressure. (15 refs.)

[No address]

2552 Finney, D.J. Placebomania and the interpretation of clinical trials. Journal of New Drugs, 1962, 2, 327-332.

Statistical interpretation of clinical trials falls prey to the following hazards: investigators inept in the more sophisticated aspects of statistical analysis, application of inappropriate statistical tests, arithmetic errors, inherent group differences, extraneous factors and failure to recognize efficacy of treatment. Other problems include an erroneous hypothesis, overcomplicated trial design, misinterpretation of

the concept of normal limits of statistical significance, true placebo versus standard therapy as an optimal control in a clinical trial and the importance of human evaluation rather than numerical manipulation. (5 refs.)

Department of Preventive Medicine
Harvard Medical School
Boston, Mass.

2553 Girard M. Traitement de la maladie de Parkinson. [Treatment of Parkinson's disease.] Journal de Médecine de Lyon 1962, 1005, 301-314.

Staples used to combat Parkinson's disease include scopolamine (0.01-1 mg/day), genoscolamine (1-4 mg/day), hyoscine, belladonna, and *Datura stramonium* extract. Newer drugs which modify extrapyramidal hypertonia include piperidine derivatives such as trihexiphenidyl (6-20 mg/day) for postencephalitic syndromes, procyclidine (10-30 mg/day), dioxopiperidine (10-30 mg/day), piperidine (4-20 mg/day) and cycrimine (1.25-2.50 mg/day). These drugs relieve hypertonia and also control tremor. Side effects include dry mouth, difficulties in visual accommodation, constipation and slight mental clouding. A number of phenothiazine derivatives such as diethazine, isothiazine, caramiphen, diphenhydramine and atropine are used in varying doses to combat tremor, but will also alleviate hypertonia. Promethazine and phenindamine, 50-100 mg/day, are used to relieve tremor. Somnolence is the most important side effect. Dexamphetamine (2.6 mg b.i.d. or t.i.d.), centrophenoquine (4-6 100 mg tablets/day) and imipramine (25 mg t.i.d.) are used to combat akinesia. Supportive therapy includes vitamin therapy, hormone therapy, ADP and insulin in small doses (10-20 U per day). Psychotherapy is of primary importance, and patients should be maintained in their normal social and occupational environments. Physiotherapy is also extremely important. Where the disease is resistant to psycho-, chemo- and physiotherapy, surgery may be indicated. Recent operations attempt to destroy the pallidal point and the pallidofugal fibers on the side opposite to that of the clinical syndrome, in particular the ventrolateral

and ventroposteriolateral thalamic nuclei. These formations can be repaired stereotactically. Surgery is contraindicated for persons over 60, those with serious vascular sclerosis, and those with obsessional or anxiety neuroses (No refs.)

[No address]

2554 Pichot, P. Remarques sur l'effet placebo: à propos des méthodes thérapeutiques en médecine psychosomatique. [Remarks on the placebo effect on therapeutic methods in psychosomatic medicine.] Acta Psychotherapeutica et Psychosomatica, 1962, 10, 75.

Symptoms, the patient and his personality, the method of presenting the placebo, the attitude of the doctor toward the efficacy of the "drug," etc., affect placebo effectiveness, leading to difficulty in precisely judging the pharmacodynamic action of drugs. (No refs.)

[No address]

2555 Held, R. Psychopharmacologie et psychothérapie en médecine psychosomatique (Introduction). [Psychopharmacology and psychotherapy in psychosomatic medicine. (Introduction).] Acta Psychotherapeutica et Psychosomatica, 1962, 10, 74-75.

Since time immemorial, treatment has depended to a good extent on the spoken word. The role of the doctor in prescribing, fears in many patients of medicines, different forms of intolerance, effective or allergic, the differences in personalities, e.g., oral, aggressive, sado-masochistic, etc. are discussed in relation to tranquilizers, neuroleptics and hypnotics, combined with psychotherapy. (No refs.)

[No address]

2556 Journal of New Drugs. Generic names of new drugs. Journal of New Drugs, 1962, 2, 188-192.

Among the newly designated generic names for drugs adopted by the AMA-United States

Pharmacopeia Nomenclature Committee are the following psychoactive drugs: pargyline, levamfetamine and hydroxyphenamate. (No refs.)

660 Madison Avenue
New York 21, N.Y.

2557 Journal of New Drugs. Generic names of new drugs. Journal of New Drugs, 1962, 2, 63-64.

Thalidomide and ampecloral are among the generic names for drugs which have recently been adopted by the AMA-United States Pharmacopeia Nomenclature Committee. Assignment of a generic name does not imply endorsement of the drug. (No refs.)

660 Madison Avenue
New York 21, N.Y.

2558 Shepherd, Michael, & Wing, Lorna. Pharmacological aspects of psychiatry. Advances in Pharmacology, 1962, 1, 227-276.

The multitudinous ramifications of pharmacology in psychiatry are based upon optimal methods of studying psychotropic drugs such as animal studies (which encompass motor functions, perception and discrimination, learning, memory and reasoning, emotion and motivation, fear and conflict), and studies in human subjects. Classification and description of psychotropic drugs include the major tranquilizers (the phenothiazines, reserpine and its congeners and the butyrophenones), the minor tranquilizers (phenothiazines and diphenylmethane derivatives), sedatives, centrally acting anticholinergics, thymoleptics (amphetamine, phenothiazine analogues and MAO inhibitors), psychotomimetic drugs (mescaline, LSD, cholinergic blocking agents and phencyclidine), transitional compounds (chlordiazepoxide and thioxanthene derivatives). Chemical interpretations of mental aberrations have resulted in proffering of postulates like the adrenaline-adrenolutin hypothesis and analogous serotonin metabolism as etiological factors in mental illness. Other relevant topics include the quantitative effects of psychotropic drugs

on humans, and the role of clinical studies related to psychotropic drugs. (287 refs.)

Institute of Psychiatry
Maudsley Hospital
London, Great Britain

2559 Committee on Public Health, New York Academy of Medicine. The importance of clinical testing in determining the efficacy and safety of drugs. *Journal of New Drugs*, 1962, **2**, 135-151.

The quest for new products led the pharmaceutical companies to embark upon research and development programs which have had almost incredible ramifications. Growth and expansion have necessitated federal controls, and the FDA once again has seen fit to impose more stringent regulations to protect the American consumer. Many profound alterations have been made in the Food, Drug and Cosmetic Act, including development of a new set of regulations for the pharmaceutical advertising industry. A report by the Professional Committee of the Pharmaceutical Manufacturers Association includes the following topics: deliberations on clinical testing, present quality of clinical testing, adequacy of supply of qualified clinical testers, utilization of available investigators, past attempts toward organization and new proposals. (28 refs.)

[No address]

2560 Friend, Dale G. Clinical evaluation of new drugs. *Journal of New Drugs*, 1962, **2**, 152-159.

In clinical testing, the nature of the drug undergoing study largely predicates the type of evaluation program which will be carried out. Once sufficient animal toxicity testing and preliminary human testing have been performed, the drug is ready to be utilized by the clinical investigator. All drug investigations in patients should be initiated in the controlled atmosphere of hospital practice. Individual subjects should be carefully determined for each preparation. Interpretation of information secured from clinical evaluation requires a high degree of

accuracy and insight. New drugs should not be introduced into medicine unless they possess definite, proven merit. (1 ref.)

Peter Bent Brigham Hospital
Boston, Mass.

2561 Marks, John. Placebomania. *Journal of New Drugs*, 1962, **2**, 71-77.

Clinical assessment of new drugs should encompass a pilot study or screening device followed by a thorough clinical trial where indicated. Controlled trials are most efficacious when double-blind or placebo methods are instituted as safeguards to maintain drug anonymity. Study designs now in vogue include the crossover, Latin square or incomplete block test. Legal and ethical problems may often be obviated in new drug testing merely by substituting standard therapy in lieu of the placebo. Placebomania results from erroneous hypotheses, incorrect criteria for assessment of results, extraneous biasing factors, excess faith in double-blind trials, complicated data collection procedures, negative effects of intervals between active drug administration, dearth of comprehension regarding statistical analysis, ignorance of randomization procedures and effects derived from standard therapy which influence trial results. Careful clinical observation will never be replaced by the placebo. (2 refs.)

[No address]

2562 Paget, G.E. Toxicity tests: a guide for clinicians. *Journal of New Drugs*, 1962, **2**, 78-83.

Toxicity tests are useful to predict what will happen when a compound is given to human beings. Such predictions may be quantitative; an estimate of what drug dosage will cause an effect, or qualitative; what effect will occur with a given dose. In animals, the only important quantitative consideration which exists in toxicity testing is the way in which animal data are to be extrapolated from species to species. Toxicity tests most readily detect severe universal poisons which are likely to cause clinical catastrophes. Regardless of how

minute the chemical difference between 2 molecules may be, each should be regarded and treated as toxicologically separate. Clinical biochemical and hematological examinations should be included in animal toxicity tests. Histological evaluation remains mandatory to detect serious morphological changes. Variation among species is a major cause of difficulty in extrapolating results from animals to man, or even between animal species. Validity is predicated upon utilization of species that are widely divergent phylogenetically. Development of a valuable new drug is invariably a cooperative endeavor between experimentalist and clinician. (7 refs.)

Imperial Chemical Industries, Ltd.
Pharmaceuticals Division
Alderley Park
Macclesfield, Cheshire
Great Britain

2563 Larrick, George P. "Our common goals." *Journal of New Drugs*, 1962, 2, 83-187.

In the interests of greater consumer protection against drug misuse which may prove dangerous or even fatal, suggestions are offered for strengthening FDA regulations on drug usage. Information concerning deleterious sequelae from drug administration is frequently withheld from the FDA by drug manufacturers, and evidence of this nature which has been brought to light through investigations has resulted in withdrawal of several drugs from the market. It is imperative that pharmaceutical houses be forced to maintain adequate facilities and controls to preclude drug contamination and recognize adverse side effects immediately. Legislative modifications are also indicated to permit suspension of a new drug where suspicion exists regarding its safety. Numerous incidents involving crimes committed under the influence of amphetamines have been recorded in the literature. Legislation must be enacted to control the illicit sale of these drugs. FDA inspectors are still seeking the right to review prescription files in pharmacies. (No refs.)

St. John's University
Jamaica, Long Island
N. Y.

2564 Sanchez F. Murias, D. Benjamin. *Tranquilizantes en medicina*. [Tranquilizers in medicine.] *Annales de la Real Academia Nacional de Medicina*, 1962, 79, 95-146.

Delay's classification and that of Lattanzi techniques of evaluation, effects on behavior (including spider web building, nest building activity in rats, aggressiveness in monkeys, induction of fear in rats and aggressiveness in monkeys, induction of fear in rats and aggressiveness of Siamese fighting fish), conditioning experiments, the study of reflexes (righting reflex, rotarod, traction, rotating cylinder, etc.), action on the lower centers of the CNS, action on the electrical activities of the brain, interaction with convulsants, morphine, lysergide (LSD), and with hypnotics and general anesthetics, the mechanism of action (relationships to 5HT), modification in oxytoxic response, interaction with novocaine and similar agents, and side effects are reviewed. (78 refs.)

[No address]

2565 *Diseases of the Nervous System*. Investigation of thalidomide deformities. *Diseases of the Nervous System*, 1962, 23, 455. [Editorial].

Dr. Charles H. Frantz, orthopedic consultant to the area Child Amputee Center of the Michigan Crippled Children Commission, Grand Rapids, Mich., has been selected to aid Germany in solving problems created by the recent birth of 3,500-5,000 thalidomide babies. He will investigate the deformities caused by thalidomide and the methods devised by German scientists in fitting infants with prosthetic devices. (No refs.)

[No address]

2566 Jerome, Joseph B. Selecting generic names for new drugs. *Journal of New Drugs*,

1962, 2, 276-282.

The A.M.A. and U.S. Pharmacopeia have established the A.M.A.-U.S.P. Cooperative Program under the auspices of a joint Nomenclature Committee to facilitate the adoption of acceptable generic names for drugs. Specific procedures must be followed, in keeping with the concepts of simplicity of generic name and maintenance of relationship in nonproprietary names in chemically related drugs used within a given therapeutic area. Manufacturers are, of course, closely consulted by the Committee in order to arrive at a decision which is suitable to all concerned. Family names like the tetracyclines, sulfonamides and penicillins present horrendous nomenclature problems which must be simplified. Some names will be retained despite their cumbersome aspects since they have been universally adopted. The general principles for guidance in devising international nonproprietary names for pharmaceutical preparations are presented in tabular form. (No refs.)

[No address]

2567 Cole, Jonathan O. Evaluation of drug treatments in psychiatry. *Journal of New Drugs*, 1962, 2, 264-275.

Close attention must be paid to all aspects of the milieu in order to assure validity in clinical trials of psychoactive drugs like chlorpromazine and reserpine, which have been in use for 10 years. Multitudinous factors influence the outcome of a given study, and all must be considered in the final evaluation. Drugs encourage far more flexibility than psychotherapy and permit utilization of biochemical changes to determine pharmacological effect. The observational acumen and clinical judgement of the investigator and his team are of paramount importance in establishing adequate evaluation procedures. Work with chronic schizophrenics poses many difficult problems. Such individuals are generally drug resistant and non-cooperative, with a poor initial prognosis. However, such patients exist in a controlled atmosphere under constant supervision. In acute schizophrenia, studies reveal few differ-

ences between several highly effective phenothiazines, chlorpromazine, thioridazine, fluphenazine, etc. Comparisons between MAO inhibitors and ECT have not produced definitive results in amelioration of depressive symptoms. Short term, double-blind, crossover studies in depressive patients have succeeded in proving nothing. Obvious problems confront the clinician involved in drug evaluation in neurotic outpatients. Measurement of clinical change includes global ratings, statistical analysis, the Wittenborn scale, Lorr IMPS, Overall-Gorham scale, MSRPP, etc. Bias exists even in double-blind methodology. Computers are invaluable in expediting data gleaned from clinical trials. Application of computer methods to EEG's should prove valuable. (39 refs.)

Psychopharmacology Service Center
NIMH
Bethesda, Md.

2568 Heller, G.C. Notes on design and methodology in psychiatric clinical trials. *The International Journal of Social Psychiatry*, 1962, 8, 55-57.

Standardization in clinical psychiatric trials is hampered by difficulties in diagnosis, personality factors, assessment of causation and trial results. Diagnostic nomenclature remains a welter of chaos. Thorough cross-matching in drug trials would vastly simplify methodology in clinical investigations. (10 refs.)

Warley Hospital
Brentwood, Essex
Great Britain

2569 Izquierdo, Iván. A model for conditioned reflexes. *Medicina Experimentalis*, 1962, 6, 281-287.

A model for conditioning and habituation of CR's based on previously obtained results in 44 "acutely conditioned" and 18 "chronically conditioned" rats, conditioned classical or instrumental means, is described, as well as interference caused by chlorpromazine used as a reference compound. The principle is predicated upon

the fact that messages emitted by a neuron are conditioned by those it receives; there are nervous structures which can be activated by some, but not all, messages; CR's require a basic plan which can be set up in dissimilar nervous areas. (28 refs.)

Cátedra de Farmacología Experimental
Facultad de Farmacia y Bioquímica
Buenos Aires, Argentina

2570 Sutter, J.M. Le danger neuro-psychiatrique des grandes thérapeutiques modernes. [Neuro-psychiatric dangers of the major modern drugs.] *Algérie Médicale*, 1962, 66, 507-512.

Psychotonic amines used as anorexigenic agents affect character, cause insomnia, and may even precipitate the onset of severe neuroses and psychoses. Reserpine or other rauwolfia alkaloids can induce, in hypertensives, depressive syndromes that verge on true melancholy. Various modern drugs (such as iproniazid, nialamide, etc.) employed in cardiology, rheumatology, and endocrinology for their analgesic properties should not be used on patients with a tendency toward psychic depression or manic excitability, etc. The gonadotropic hormones can change behavior patterns, while corticoids can induce either agitation or depression. Antitubercular drugs such as isoniazide can induce convulsions or polyneuritis, while others may be responsible for convulsions or vertigo. Even vaccinations entail the risk of encephalitis. Effects of drugs may differ from adults to children. Toxicomania may result from ingesting products like amphetamine. Prolonged use of other drugs such as tranquilizers may result in addiction. Children respond more directly to treatments involving pain, such as lumbar punctures, or hospitalization, removing the patient from the family. (No refs.)

[No address]

2571 Borenstein, P., Dabbah, M., & Blès, G. Note à propos du potentiel épileptogène éventuel de deux anti-dépresseurs: 1) le P. C. 603, inhibiteur de la mono-amino-oxydase; 2) l'aminotryptiline, dérivé des dibenzo-cyclo-heptadiennes. [Note on the epileptogenic potential of 2 antidepressants:

PC 603, a monamine oxidase inhibitor, and amitriptyline, a derivative of the dibenzocyclo-heptadines.] *Annales Médico-Psychologiques*, 1962, 120, 1, 144.

Improvement in basic EEG rhythm in depressive states, absence of clinical epileptic seizure provoking activity, the appearance or aggravation of generally transitory abnormalities in the EEG tracings of epileptics with an absence of correlative aggravation in the clinical picture are noted for both amitriptyline and PC 603 (p-chlorophenoxyacetic isopropylhydrazine) [dosages unspecified]. The problem of criteria of psychotonic activity in the EEG is still current. EEG aggravations caused by psychotonics, however transitory and fluctuating, are often paradoxically in opposition to successful clinical results. (No refs.)

[No address]

2572 Northwest Medicine. Thalidomide. 1962, 61, 651. [Editorial]

The recent tendency toward more stringent drug regulations resulting from the thalidomide furor is decried on the basis of the deleterious effects of excessive governmental intervention in industry. Invectives are hurled at the President, Dr. F. Kelsey, and the government in general. (No refs.)

Northwestern Medicine
500 Wall St.
Seattle 1, Wash.

2573 Soulairac, A., Halpern, B., Grisoni, F., Brunhès, M., Frélot, Cl., Geier, S., & Ochonisky, J. Intérêt des échelles de J.R. Wittenborn en recherche clinique psychiatrique. [The Wittenborn scales in clinical psychiatric research.] *Annales Médico-Psychologiques*, 1962, 1, 354-389.

Use of the Wittenborn scales as an aid in the objective description of psychic states and the effect of various drugs upon them is illustrated by profile for 5 examples out of 31 schizophrenics who had received various treatments [dosages unspecified] and were subsequently treated with chlorprothixene, followed by haloperidol therapy. Condition composed were: profile before

treatment, after a month of chlorprothixene, a month after the chlorprothixene therapy and 3 out of the 5 cases after 1 month of haloperidol. These profiles indicate that objectivization of clinical observation is possible and useful in treating psychic stages. (5 refs.)

Centre Psychiatrique Ste-Anne,
Paris, France

2574 Borel, A. Champignons, noyau indolique et psychisme. [Mushroom, the indole nucleus and psychism.] *Journal des Sciences Médicales de Lille*, 1962, 80, 119-130.

Amanita muscaria is toxic but generally not fatal. It induces disturbances of vision, auditory and visual hallucinations, amnesia, gait, and affects the parasympathetic system. Mexican hallucinogens include peyotl, *Datura* sp., *Rivea corymbosa* and *Sophora secundiflora*, as well as various *Psilocybe* and *Stropharia*. The active principles of these drugs have been isolated by extraction and analyzed chromatographically. These are 4-hydroxy-dimethyl tryptamine, and the phosphorylated derivatives of this compound (in position 4). Psychic effects include visions consisting of garish sights overlaid on steep streets and buildings. Ability to think and to remember is only slightly affected. *Panaeolus fungi* have similar effects. LSD, at doses of 0.5-2 mg/kg creates agitation, vertigo, semi-ebriety, characterized by extreme activity of the imagination. LSD had an indole structure. Dimethyltryptamine is hallucinogenic, as are also various methyl tryptamines, and also those derivatives which are obtained by phosphorylation on the 4th carbon atom. 5HT (serotonin), which is also an indole compound, may induce hallucinations and convulsions by slowing oxygen passage through the brain. Both LSD and psilocybin are used in anxiety neuroses and obsessive states for the facilitation of recall, particularly of early childhood traumas.

[No address]

2575 Lange, P. Über die Rolle der γ -Aminobuttersäure im Zentralnervensystem [The role of GABA in the central nervous system.] *Zeitschrift für Ärztliche Fortbild-*

ung, 1962, 4, 233-237.

GABA exercises an inhibiting effect on the stretch receptor neurons. Intravenous doses as low as 0.1 mg/kg GABA affects feline pulmonary stretch receptors. Effects are proportional to doses. Changes in the brain bioelectric potential in dogs can be noted only at 400-500 mg/kg GABA, administered i.v. Intracisternal administration of GABA will inhibit muscle movements induced by the application of strychnine to the brain cortex, but the "strychnine spikes" in the EEG's are not altered. Administration of thiosemicarbazide in lethal doses leads to a 30% reduction of the GABA content in the brain. Similar results were obtained with other convulsion-inducing compounds. Other substances, e.g., hydroxylamine in doses of 4.8 mg/kg increase GABA content and reduce cerebral excitability, GABA is an important constituent of the so-called "metabolic pool" which plays a role in the regulation of excitability. (90 refs.)

Institut für Pharmakologie der Deutschen
Akademie der Wissenschaften
Berlin-Buch, Germany

2576 Northwest Medicine. 2-PAM. Northwest Medicine, 1962, 61, 652. [Editorial]

2-PAM (2-pyridoxine aldoxime methiodid) reactivates cholinesterase after organic phosphates which cause hyperacetylcholinism. The compound is advocated as a substitute for atropine 2-PAM reactivates cholinesterase. (3 refs.)

Northwestern Medicine
500 Wall St.
Seattle 1, Wash.

2577 Mark, Lester C. Analeptics: outmoded therapy of barbiturate poisoning. *Anesthesiology*, 1962, 5, 713-714. [Editorial]

There is no safe antidote for barbiturate poisoning. Mortality figures can be drastically reduced (with good recovery through care and no analeptics). Patients who reached the hospital alive have withstood the primary onslaught and are no longer in imminent danger of death from the ingested

drug per se. It is ill conceived to administer an analeptic toward off nonexistent hazards. Cardiorespiratory complications are now the menace to be controlled by symptomatic management of the comatose patient. Efforts have shifted from desperate efforts at arousal to an orderly regime of supportive therapy. (No refs.)

[No address]

2578 Subramaniam, M. Pharmacotherapy in psychotic disorders. Medical Journal of Malaya, 1962, 17, 25-36.

After presenting a simplified classification (neuroleptics, psychoneuroleptics, and psychotomimetics), chlorpromazine, trifluoperazine, phenelzine, prochlorperazine, amphetamine, imipramine, MAO inhibitors, iproniazid, phenelzine, pheniprazine, isocarboxazid, tranylcypromine and nialamide are discussed, primarily in relation to dosage, secondarily in concern with side effects. Some drugs require higher dosages for longer periods of time than commonly expected for good results. (15 refs.)

Central Mental Hospital
Malaya

2579 Carpenter, John A. Effects of alcohol on some psychological process. Quarterly Journal of Studies on Alcohol, 1962, 23, 274-214.

In relation to alcohol ingestion, reaction time, motor skills, positional nystagmus, sensory processes, intellectual functions, tests of driving skill, validity of driving tests, subject variability and methodological questions are reviewed. Original articles and the Classified Abstract Archive of the Alcohol Literature were surveyed. The traditional idea that intellectual functions are particularly susceptible to deterioration by alcohol is questioned. Alcohol impairs automobile driving performance at low blood alcohol levels according to all reports. Positional nystagmus, appeared to be strongly related to the presence of alcohol in the blood, and to hangover. Little creative effort has been spent in this area of human behavior. (79 refs.)

Center of Alcohol Studies
Rutgers University
New Brunswick, N. J.

2580 Remmen, Edmund, Cohen, Sidney, Ditman, Keith S., & Frantz, John Russell. Psychochemotherapy. The Physician's Manual. Los Angeles: Western Medical Publications, 1962, Pp. 152.

This book is written as a guide to the general practitioner. Mental illness, the classification and diagnosis of mental illness, modern concepts on its biochemical nature and information on psychotropic drugs are presented. Copious miscellaneous information is detailed on diagnostic aids and sites of drug action with an emphasis on dosage schedules for patients in private practice. (317 refs.)

Western Medical Publications
Los Angeles, Calif.

2581 Brooks, Clyde. The new role of the general practitioner in the treatment of mental cases with the new psychobolic drugs. Louisiana State Medical Society, 1962, 114, 291-293.

Tranquilizers should be renamed psychobolic drugs, a classification which encompasses reserpine and thioridazine as typical examples. Improvements in psychiatric training will result in greater treatment of mental patients on an outpatient basis. Reserpine (2.5 mg/ml parenterally) is advocated as the drug of choice, despite side effects which include slow pulse and hypotension. Mental patients may be treated by psychotherapy, ECT or medical therapy, including psychoactive drugs. Maintenance therapy with reserpine (2-4 mg/day p.o. interspersed with 5 mg i.m., b.i.d.) is highly efficacious. (No refs.)

Alabama State Hospitals
Tuscaloosa, Ala.

2582 Dorfman, Wilfred. Depression and psychosomatic illness. Southwestern Medicine, 1962, 43, 195-197.

Obesity, coronary disease and rheumatic disorders are cited as conditions which may coexist with depression. In relation to treatment, the 2 major factors are the nature of the depression and the orientation etc. of the therapist. ECT, psychotherapy and pharmacotherapy all have their exponents. Neurotic or reactive depressions are best handled by psychotherapy. In some cases antidepressants may act as synergists in psychotherapy and provide greater acceptability. Some of the new drugs can eliminate ECT or cut down the number of treatments. These newer drugs include phenelzine, isocarboxazid, nialamide, imipramine and amitriptyline. Amitriptyline is preferable when high levels of anxiety accompany the depression. Difficulties in drug evaluation are noted. (10 refs.)

Department of Psychiatry
Maimonides Hospital of Brooklyn
Brooklyn, N.Y.

2583 Lasagna, Louis. Some explored and unexplored psychological variables in therapeutics. *Proceedings of the Royal Society of Medicine*, 1962, **55**, 773-776.

Considerable psychological variation accounts for discrepancies in response to various medication. Most healthy volunteers treated with amphetamine or opiates are euphoric and mentally stimulated by amphetamine but a minority react with depression and sedation. Differential responses to morphine and heroin follow an analogous pattern. The toxicity of CNS stimulants is markedly enhanced in animals placed in a crowded environment. A doctor's tendency to innovate is based upon his individuality and his social position among other doctors. Psychological and sociological variables must be taken into consideration in drug evaluations. (20 refs.)

Johns Hopkins University
School of Medicine
Baltimore, Md.

2584 Gerecke, K., & Koch, K. Über den Verkehr mit Betäubungsmitteln. IV. Mitteilung. [Traffic in narcotics. IV. Communication.] *Pharmazie*, 1962, **12**, 205-214.

The extensive review is based on international and German reports on opium, opium derivatives, and synthetic addicting analgesics. Thirteen tables and 5 graphs describe production and processing, medical and other uses, import and export, and illegal traffic. (112 refs.)

Grosse Seestrasse 4
Berlin-Weissensee, Germany

2585 Christian, Joseph R. Drug and chemical poisonings and their management. *Medical Science*, 1962, **12**, 37-46.

Fourteen-hundred to sixteen-hundred fatal poisonings occur each year in the U.S.A. and almost 80% of these fatalities occur in the age group 1-4 years. Non-fatal poisonings may occur 100-200 times more frequently than fatal poisonings. Immediate first aid measures for all types of poisonings, diagnosis, management of common poisoning (1. aspirin; 2. barbiturates; 3. lye and corrosive alkalis; 4. hydrocarbons; 5. tranquilizers - chlorpromazine, reserpine, meprobamate; 6. carbon monoxide; 7. ferrous and ferric compounds; 8. atropine and belladonna, and 9. pesticide - insecticide-herbicide group) and a discussion on lead poisoning is provided. (No refs.)

University of Illinois
College of Medicine
Chicago, Ill.

2586 Medical Science. *Collegium Internationale Neuropsychopharmacologicum*. *Medical Science*, 1962, **12**, 985-990. [Editorial]

A discussion "Methods of comparison of behavior changes with drugs in animals and man" opened the Third Congress of the Collegium Internationale Neuropsychopharmacologicum, attended by 400 scientists (Munich, September, 1962; under the chairmanship of President Paul Hoch). Methods of testing, the role of tranquilizers and antidepressants, the need for drug therapy in psychoses, ethnic differences in drug response, and the history of psychopharmacology were discussed. Dr. F. Ayd reported that chlorpromazine has been

prescribed for at least 50 million people and that it has been the subject of or mentioned in over 10 thousand scientific publications. (No refs.)

227 S. 6th St.
Philadelphia, Pa.

2587 Dell, P. Effets centraux éveillants de l'adrénaline et de leurs précurseurs. [Central pressor effects of epinephrine (adrenalin) and its precursors.] *Thérapie*, 1962, **17**, 329-334. [Discussion]

The central effects of circulating epinephrine and levarterenol (adrenalin and noradrenalin), and the functional role of catecholamines localized at the level of the brain stem and the relationships to the total activity of an organism are reviewed. Also the effects of MAO and COMT inhibitors are discussed by Dell, Beauvallet, Minz, Barbizet, Jacob, Schmitt, Lévy and Cheymol. (No refs.)

[No address]

2588 Kalant, Harold. Some recent physiological and biochemical investigations on alcohol and alcoholism. *Quarterly Journal of Studies of Alcohol*, 1962, **23**, 52-89.

Extensive perusal of the literature pertaining to alcoholism reveals the mechanisms involved in alcohol metabolism, the pathways, enzymes, tissues, rate limiting factors and drugs. Recent literature concerned with alcohol effects on the CNS includes controversial studies of effects of alcohol on respiration of brain slices in vitro and alterations in brain constituents under alcohol effects in vivo. Studies on the reticular formation demonstrate the effects of alcohol upon integrated neurological function in living subjects. Other topics include the role of alcohol in relation to stress, anxiety, endocrine functions, liver fat formation, liver function and development of cirrhosis. Many investigations deal with differences between normal subjects and alcoholics in regard to anxiety, biochemical and physiological changes. Alcoholism is currently treated empirically by means of tranquilizers, disulfiram, cal-

cium carbimide and antidiabetic sulfonamides like tolbutamide. (28 refs.)

Alcoholism and Drug Addiction Research
Foundation
Toronto, Ontario
Canada

2589 Gerscovich, José. Sub-coma insulínico. [Insulin sub-coma.] *Revista Brasileira de Medicina*, 1962, **19**, 684-686.

The history of insulin coma therapy is presented and contrasted to the technique of insulin sub-coma therapy. Objectives, contraindications (cardiac, hepatic or renal disorders, or diabetes) clinical and laboratory test preparation for treatment, adjunct and the technique itself, as well as complications and secondary shock are elucidated. (No refs.)

Sociedade Brasileira de Psiquiatria,
Neurologia e Medicina Legal
Rio de Janeiro, Brazil

2590 Medical Science. Poisons and Mental Function. *Medical Science*, 1962, **12**, 64-69. [Editorial]

Compounds such as atropine, scopolamine and some related synthetic drugs used in the treatment of parkinsonism cause mental and behavioral abnormalities through their effect on acetylcholine. On the other hand, substances like physostigmine, diisopropyl fluorophosphate and some weed killers increased acetylcholine amounts by inhibiting or destroying cholinesterase, and these caused similar mental changes. Chronic heavy mental poisoning, e.g., mercury, may also mimic endogenous psychiatric disorders. Unsaturated indoles can cause depersonalization and sometimes hallucinations. One of these, LSD, occurred in ergot, the fungus which grows on rye. Carelessly made rye flour may cause epidemics of psychosis among those who eat the bread made from it. Bufotenin and its phosphate ester psilocybin are also unsaturated indoles, occurring in mushrooms. Another of this type is harmine, related to reserpine and yohimbine. Adrenolutin is also an unsaturated indole that

causes mental changes; spoiled epinephrine contains it. When sprayed into the airways in large amounts it may produce psychosis. The nonindolic hallucinogens, mescaline and marihuana, are noted. Barbiturates may cause excitement and confusion, particularly in elderly patients. Adrenosteroids often cause some degree of euphoria and may in some instances produce melancholia or schizophrenialike psychoses. Commonly used tranquilizers may cause severe stubborn depressions, e.g., the prolonged use of reserpine in hypertension. (No refs.)

227 S. 6th St.
Philadelphia, Pa.

2591 Connell, P.H. The amphetamines - I. Medical World, 1962, 96, 18-20.

Amphetamines in clinical use today include ephedrine, epinephrine, levarterenol, deoxyphedrine and phenmetrazine. Related compounds which are effective anti-depressants include nialamide and tranlylcypromine. Metabolic pathways remain nebulous, but relatively large amounts of the original dose are excreted unaltered in the urine. All amphetamines exert a general stimulating effect on the CNS coupled with a euphoriant action, appetite suppression and narcotic antagonism. Amphetamines appear to effect the reticular arousal system in the brainstem. Mild, undesirable side effects include dry mouth, insomnia, palpitations, headache, impotence, etc. With regard to CNS activity dexamphetamine is the most potent compound. (No refs.)

Newcastle General Hospital
Newcastle-on-Tyne Great Britain

2592 Hope, Justin M. The anxiety state. Medical World, 1962, 96, 9-15.

Anxiety states encompass periodic acute attacks, headache, nervousness, palpitation, irritability, diffuse fear, sexual maladjustment, choking or smothering, trembling, precordial or chest oppression, dizziness, precordial or chest pain and fainting. Few positive findings are detected by physical examination. Anxiety is of unknown etiology. Differential diagnosis must include

medical problems (coronary heart disease, thyrotoxicosis, etc.), gynecological, neurological and psychiatric disorders. Chronic anxiety may be alleviated by amylobarbitol (0.5-.75 grains t.i.d.), meprobamate (200-400 mg q.i.d.), chlordiazepoxide (5-10 mg q.i.d.) and phenobarbital i.m. (No refs.)

New England Center Hospital
Tufts University School of Medicine
Boston, Mass.

2593 Greeves, J.A. Post-partum psychiatric illness in general practice. Medical World, 1962, 97, 104-107.

Postpartum complications include puerperal anxiety state, puerperal psychosis, affective syndromes (depression and mania) and schizophrenic syndromes. Early separation of mother and child resulting from such disorders may result in a heightened feeling of rejection on the part of the child. Imipramine, chlorpromazine (75-100 mg t.i.d.) and phenelzine may prove efficacious in these unfortunate sequelae. (No refs.)

Department of Psychological Medicine
University College Hospital
London, Great Britain

2594 Tissot, R. Monoamines et système nerveux central. [Monoamines and the central nervous system.] Presse Médicale, 1962, 70, 1352-1354.

The study of levarterenol, 5HT and dopamine, present in the CNS, is difficult because of the blood-brain barrier. The role of MAO and MAO inhibitors (potent antidepressants) is discussed. The mobilization of catecholamines by reserpine and its central actions are fundamental to any discussion. These studies constitute the pillars on which psychopharmacology has been built in the last decade. (2 refs.)

Clinique Universitaire de Psychiatrie de Genève
Geneva, Switzerland

2595 Leder, Stefan. Treatment of neurosis. Medical World, 1962, 97, 9-13.

Neuroses may be treated by simple supportive psychotherapy or complex therapy combining supportive therapy with drug therapy. Rapport must first be established with the patient, after which supportive therapy may be instituted. Hypnosis may be useful in the hands of an experienced therapist. Systematic therapy involves lengthy analytic procedures which lead to an attitudinal and behavioral metamorphosis. Complex therapy utilizes drugs, hormones, amobarbital and nitrous oxide inhalations, occupational therapy and even physiotherapy to insure successful treatment. (No refs.)

Institute of Psychoneurology
Pruszkow, Poland

2596 Forsander, Olof A. Metabolic tolerance to alcohol as a possible limiting factor in its consumption. Quarterly Journal of Studies on Alcohol, 1962, 23, 480-482.

Animal experiments where the test animal is given a free choice between water and an alcohol solution cannot be correlated to factors involving alcohol consumption in man. These experiments are valid if they are correlated to a limitation of alcohol consumption instead of to a craving for alcohol. Every animal species investigated has shown a relatively constant daily alcohol consumption. Metabolic tolerance, limitation of ability to consume alcohol, has nothing to do with the forces that drive a person to drink, but if an individual with a high metabolic tolerance to alcohol drinks heavily, metabolically speaking he is a potential alcoholic. Metabolic tolerance is difficult to investigate. Man always has a socially or morally colored attitude towards alcohol. (8 refs.)

Research Laboratories of the State Alcohol Monopoly
Helsinki, Finland

2597 Jepson, William W. Management of acutely disturbed patient. Minnesota Medicine, 1962, 45, 1010-1012.

In almost all instances of acute disturbance, a fundamental etiological factor is that the patient himself is very frightened or even panicky. Those around the patient may demand that the doctor "do something immediately." The physician's role is to allay anxiety and establish trust. One first step is getting him to assent to some medication such as 3.75-7.5 grains of amobarbital or $\frac{1}{4}$ grain of morphine i.m. After some quieting, 25-50 mg chlorpromazine is useful; blood pressure should be observed and the patient watched for a hypotensive reaction. The synergism between a barbiturate and a phenothiazine is useful. If force is indicated, a show of force may suffice. The legal status of the doctor is noted. (No refs.)

Minneapolis General Hospital
Minneapolis, Minn.

2598 Lesse, Stanley. Placebo reactions in psychotherapy. Diseases of the Nervous System, 1962, 23, 313-319.

Placebo reactions in general encompass pure placebos (inert compounds), placebo (drug or procedure), placebo effect (reaction), and positive or negative placebos. The largest and most enduring number of positive placebo reactions are obtained by physicians who are optimistic and promulgate strong convictions with regard to the anticipated positive response to be elicited from a given drug or procedure. A similar patient attitude is instrumental in evoking this positive response. The forces which determine manifestation of a placebo reaction play a vital role in determining the final results in any psychotherapeutic procedure. In evaluation procedures, the question of spontaneous remissions must also be considered. (No refs.)

Neurological Institute of New York
Department of Neurology
Columbia University
New York, New York

2599 Rice, Carl O. Tranquility and tranquilizers. Minnesota Medicine, 1962, 45, 1025. [Editorial]

Reviews
Abstracts 2600-2604

Before the advent of tranquilizers, the word tranquility meant a calm state of mind. Now the search of tranquility appears to be the province of neurotics, psychopaths and others of unstable makeup. Perhaps the individual for whom tranquilizers are often prescribed is normally and temporarily distraught at various life situations. (No refs.)

[No address]

2600 Connell, P.H. The amphetamines - II. Medical World, 1962, 96, 106-111.

Amphetamines are used clinically for narcolepsy, parkinsonism, epilepsy, barbiturate poisoning, drug addiction, alcoholism, psychopathic states, behavior disorders in children, enuresis and depression. Drugs should be administered in a manner which minimized side effects and all patients should receive frequent reassessments. The most serious consequence of amphetamine administration is addiction. Other side effects include a "schizophrenic type" of psychosis, shock and collapse and the omnipresent risk of suicide. Amphetamine toxicity resembles alcohol intoxication and should not be so misdiagnosed. A hypersensitivity to sympathomimetics or any condition encompassing Reynaud's phenomenon contraindicates amphetamine administration. (15 refs.)

Newcastle General Hospital
Newcastle, Great Britain

2601 Aldridge, M.S. Open Way Psychotherapy Clinic. Medical World, 1962, 96, 463-467.

The Open Way Clinic in London, England provides expert psychotherapy at low cost, with an analytically oriented staff, objective attitude and emphasis on drug utilization combined with psychotherapy. Drugs like chlorpromazine are essential adjuncts to other types of therapy. Psychotherapy is never used merely for the purpose of placation. Most patients pay a minimum fee and attend the clinic twice a week. Similar clinics are sorely needed.

Open Way Psychotherapy Clinic
London, Great Britain

2602 Cunningham, John J. Alcoholism. Minnesota Medicine, 1962, 45, 1029-1035.

The incidence and nature of alcoholism, alcoholism, alcohol addiction, withdrawal signs and symptoms and treatment are reviewed. Adrenal cortex extract in delirium tremens, with later suppression of craving for alcohol is cited, along with the use of glutamine as a nutritional supplement, again suppressing the urge to drink. (No refs.)

[No address]

2603 Romano, John. Psychiatric research and medicine. Medical World, 1962, 96, 281-287.

Psychiatric research appears to lag behind that undertaken in other areas of medicine. Psychiatric training aids fledgling physicians to achieve a higher degree of insight and critical perceptiveness. Psychiatry has contributed much to medicine, particularly psychoanalytic theory, where the unitary concept and team approach have been very valuable. The family doctor eases patients through the many crisis periods in their lives. The functions of the family doctor are diagnostic and judgmental, preventive, therapeutic, integrative, investigative and educational. The prevailing tendency to rely on tranquilizers as panaceas must be critically scrutinized. Treatment of psychotics with insulin shock, ECT, pentetrazol chemical sleep has not produced direct therapeutic benefit, except for ECT in depression. While more understanding of neural organization is needed, there is evidence of beginning relatedness in studies in animals and men between behavior, learning etc.

University of Rochester
Rochester, N.Y.

2604 Sussex, James N. Drugs used in psychiatric treatment. Medical Record and Annals, 1962, 55, 225-229.

Drugs which alleviate morbid anxiety include phenothiazines, such as chlorpromazine (200-800 mg/day), thioridazine and trifluoperazine (1-8 mg/day). Parkinsonian side effects often accompany chlorpromazine administration. The phenothiazine tranquilizers enable schizophrenics to alleviate fear and suspicion, thus augmenting their ability to communicate with the physician in charge. (No refs.)

Department of Psychiatry
University of Alabama School of Medicine
Birmingham, Ala.

2605 Hill, Harris, E. The social deviant and initial addiction to narcotics and alcohol. *Quarterly Journal of Studies on Alcohol*, 1962, **23**, 562-582.

Addiction to alcohol or opiates is predicated upon drug availability, deficient social controls which fail to preclude experimentation with drugs, fortuitous circumstances which dictate the drug of choice, insufficient ego reinforcement from daily activities, and the conditioning and learning process which precedes and accompanies early phases of addiction. Repetition of the initial drug experience is contingent upon the interaction of specific drug effects with individual idiosyncratic responses and relief of abstinence symptoms after repeated use. Measurable signs of physiological dependence predispose toward relapse. (51 refs.)

NIMH, Addiction Research Center
Public Health Service Hospital
Lexington, Ky.

2606 Wagner, G. Die Entwicklung des Arzneischatzes auf dem Gebiet der Sedativa und Hypnotica. [The development of evaluation of an arsenal of drugs in the sphere of sedatives and hypnotics.] *Pharmazeutische Zentralhalle*, 1962, **101**, 3-7.

Tertiary alcohols containing an acetyl group have gained acceptance as sedatives and hypnotics since 1951. Introduction of other unsaturated components together with halogenation provide still more effective com-

pounds. Carbromal is an acylated urea, and is still used as a sedative. However, diethylacetamide and carbamide compounds can, if used over a long time, produce confusion and other difficulties. Barbiturates are highly effective and new ones are constantly being added. Barbiturates may be divided into four classes, based upon the duration of their effects: long-acting, average duration, short and ultra-short. Tolerance is increased by changes in the barbituric acid ring proper. Administration methods of various sedatives and hypnotics has been improved through the development of the sustained-release tablets. Tranquilizers are a development of the 1950's, meprobamate being the most prominent example. Phenothiazines and reserpine are detailed. Work with antihistamines has led to the development of phenothiazines with psychosedative effects. While psychotherapeutic drugs are extremely valuable they should be dispensed with proper precautions as prescription drugs, and not as over-the-counter items. (No refs.)

[No address]

2607 Hoch, Paul H., & Zubin, Joseph. [Eds.] *The future of psychiatry*. New York: Grune & Stratton, 1962. Pp. 1-271.

Multiple disciplinary cooperation in psychiatry is stressed. Neurochemistry may in the next decade further the understanding of behavioral disorders. More objective criteria are becoming available in the experimental laboratory which supplement the judgement of the clinician. Various new techniques and electronic devices are now promoting progress in psychiatry, and particularly in psychopharmacology. The 4 parts of the book are entitled: future of neurophysiologic and neurochemical approaches; future of psychologic, social and educational approaches; future of conceptual systems; and future of genetic, developmental, and organic approaches. (313 refs.)

Department of Mental Hygiene
State of New York
New York, N.Y.

2608 Evarts, Edward V. Speculations concerning future applications of neurophysiologic techniques to psychiatric research. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 1-10.

Previously, psychiatric problems have been refractory to solution by neurophysiological techniques, but these same techniques, especially the EEG, have been successfully applied to research on behavioral disturbances. Very revealing studies have been performed concerning evoked responses in patients with behavioral disorders. The EEG permits detection of electrical periodicities, which in turn may be correlated with relevant behavior. Much information has been gleaned from evoked potentials in animals using LSD, chlorpromazine and reserpine. (18 refs.)

Laboratory of Clinical Science
NIMH
Bethesda, Md.

2609 Waelsch, Heinrich. The future of neurochemistry and psychiatry. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 11-18.

The biochemist is searching in the mentally ill patient for metabolic reactions concomitant with mental phenomena. General reactions such as energy metabolism and specialized ones such as the metabolism of nitrogen compounds and nucleic acids or lipids are of special interest, e.g., the work of Rolf Gjessing on nitrogen metabolism in periodic catatonia. Much of the future biochemical research in psychiatry will be taken up by the search for abnormal metabolites and hypotheses involving the inborn errors of metabolism. Pharmacology and psychopharmacology will become a branch of neurobiology once they are able to interpret drug action in terms of changes in cellular metabolism. (7 refs.)

New York State Psychiatric
Institute
New York, N.Y.

2610 Marrazzi, Amedeo S. The influence of the experimental laboratory on psychiatry towards the turn of the century. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 19-34.

Concepts and models relating to the rational bases of cerebral dysfunction and resultant mental disturbance which focus on the disruption of homeostasis at the synaptic level are outlined. There is a likelihood that clues on the operation of genetic influences will be found in the metabolism of neurons concerning the intricacies of receptor protein formation, the choice of metabolic pathways for energy consumption, endocrine and vitamin-coenzyme systems. Greater skill in techniques, e.g., electric recording in a single neuron, combined with refinements of chemical theory and analysis can be expected to bring the correlation of structure and function nearer to the molecular level. The utility of LSD and other psychotomimetics is also underlined. Aided by neurophysiologic and neuropharmacologic maneuvers and by the pathognomic tests of responsiveness to special drugs, the psychiatrist has returned to an emphasis on diagnosis of the form of mental disease and the exact status of the illness. (18 refs.)

VA Research Laboratory in
Neuropsychiatry
Pittsburgh 6, Pa.

2611 Rioch, David McK. The future of psychiatry from the standpoint of physiology. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 35-50.

The psychiatrist will eventually become a practicing, clinical experimentalist, using objective criteria to supplement clinical judgment. Interpretation of psychosis as a failure of cerebral homeostasis at the regional and synaptic levels has served to promote amalgamation of somatic and psychic viewpoints. Utilization of neurophysiologic, neuropharmacologic maneuvers and pathognomonic tests of responsiveness to drugs like LSD and mescaline, the psychiatrist has begun to emphasize

the form and exact status of mental illness. (23 refs.)

Division of Neuropsychiatry
Walter Reed Army Institute of Research
Washington 12, D.C.

2612 Lewis, Nolan D.C. Reflections on the past, present and future of psychiatric progress. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 147-80.

Past achievements in psychiatry have progressed from the primitive or ancient period (5000-600 B.C.) through the Grecian and Roman periods, the Dark Ages, Feudalism, the Renaissance, the Reformation, individualism, the period of systems, humanitarianism and the anatomical-physiological period in order to reach the present scientific plateau. The analytic-psychologic pharmacologic era has been characterized by utilization of a combination of psychotherapy and drugs like chlorpromazine and the antidepressants. Much future work remains to be delineated. (23 refs.)

N.J. State Bureau of Research in
Institutions and Agencies
Trenton, N.J.

2613 Greenblatt, Milton. The future of psychiatry: biologic aspects. In: Hoch, Paul H., & Zubin, Joseph [Eds.] The future of psychiatry. New York: Grune & Stratton, 1962. Pp. 224-241.

Psychiatry will ultimately be able to transpose all of the work on classical and operant conditioning, reduction of experience to mechanistic terms, physiological postulates on emotional expression, interaction and social behavior and psychotherapy into the realm of dynamic psychopharmacology. Drugs like LSD and the phenothiazine derivatives are already revealing new frontiers of insight and are dramatically alleviating mental illness. (73 refs.)

Massachusetts Mental Health Center
Boston, Mass.

2614 Roessler, Robert, & Greenfield, Norman S. [Eds.] Physiological correlates of psychological disorder. St. Paul: University of Wisconsin Press, 1962. Pp. 1-281.

The papers in this volume were originally presented at a conference entitled "Physiological Correlates of Psychological Disorder" held at the University of Wisconsin, August 29-31, 1961. Reports are included from laboratories studying the relationship between intermediate carbohydrate metabolism and schizophrenia, adrenocortical function and anxiety, autonomic nervous system variables and psychological measures, and from laboratories active in elucidating psychological factors in somatic disease. Abstracts for 11 of the 15 chapters are presented in this issue of Psychopharmacology Abstracts, i.e., those chapters dealing with psychoactive drugs. (481 refs.)

Department of Psychiatry
University of Wisconsin Medical Center
Madison, Wisc.

2615 Malamud, William. Introduction: major trends in twentieth-century psychiatric research. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] Physiological correlates of psychological disorder. St. Paul: University of Wisconsin Press, 1962. Pp. 3-11.

Cannon's concept of homeostasis, defined as a mechanism which enables organisms continually subjected to wide environmental variations to maintain a constancy of conditions within their own systems, offers a natural basis for the study of physiological correlates of psychological disorder. (11 refs.)

[No address]

2616 Tourney, Garfield, Frohman, C. E., Beckett, Peter G.S., & Gottlieb, Jacques S. Biochemical mechanisms in schizophrenia. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] Physiological correlates of psychological disorder. St. Paul: University of Wisconsin Press, 1962. Pp. 13-28.

Biochemical investigations on intermediary carbohydrate metabolism in schizophrenics and control subjects reveal significantly higher ATP turnover rates in schizophrenics, coupled with an inability to mobilize ATP as an adaptive response to an insulin stressor. Findings for specific ADP activity paralleled those for ATP. The AMP levels of chronic schizophrenics were significantly lower under basal conditions than those of controls. Further metabolic studies indicate that more glucose is metabolized by Emden-Meyerhof glycolysis than via the monophosphate shunt. Schizophrenia may actually be identified biochemically on the basis of results obtained from the lactate-pyruvate ratio for chicken erythrocytes incubated with glucose. The elusive plasma factor isolated from schizophrenics is an α -globulin or a prosthetic group attached to an α -globulin. (14 refs.)

College of Medicine
Wayne State University
Detroit, Michigan

2617 Ax, Albert F. Psychophysiological methodology for the study of schizophrenia. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 29-43.

Biochemical measures and physiological variables related to the autonomic nervous system were examined in schizophrenics by means of the polygraph, GSR, ballistocardiograph, etc. Most schizophrenics do not evidence an epinephrine-like response to the stress of pain apprehension. Far more work is indicated to insure validity of statistical variables. Sensory deprivation studies pose the question of whether schizophrenia constitutes a distortion of self perception or environmental perception. Recent work utilizes the polygraph to study empathy. (27 refs.)

Lafayette Clinic and College of Medicine
Wayne State University
Detroit, Michigan

2618 Doust, J.W. Lovett. Consciousness in schizophrenia as a function of the peripheral microcirculation. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 61-96.

In conjunction with an extensive review of the literature, the following subjects were discussed: consciousness and psychology, consciousness disturbances in schizophrenia, anatomic and physiologic neural mechanisms involved in consciousness and its dysplasia in schizophrenia and spontaneous activity of the reticular formation, consciousness and the microcirculation. Studies on microcirculation in schizophrenics encompassed 2 monitors: skin temperature and spectroscopic oximeter, which were correlated with concomitant behavior and speech records plus state of consciousness. This work is predicated upon the assumption that skin temperature reflects arteriolar and metarteriolar blood flow while oximetry provides an estimate of capillary blood-oxygen saturation, suggesting a periodically operating shunting mechanism acting through a system of sphincters which are neurogenically mediated under some centrally located pacemaker control. Levels of awareness were altered by administering hydrazine, neutra-phylline, chlorpromazine and trifluoperazine. Behavioral changes were readily correlated with the above described responses. (116 refs.)

Department of Psychiatry
University of Toronto
Toronto, Ontario
Canada

2619 Wenger, M.A. Some problems in psychophysiological research. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 97-114.

Factorial analysis of data is imperative in psychophysiological research if any degree of validity is to be attained. Studies designed to determine GSR yielded widely divergent results when continuous current

was used rather than intermittent current. In groups tested for response to cold-pressor stimulation, 5 uncontrolled variables existed (time of testing, initial room temperature, external temperature, lowest relative humidity and highest barometric pressure in the 24 hours prior to testing). Other variables must, of course, be added to the correction equation to facilitate accuracy. (29 refs.)

Department of Psychology
University of California
Los Angeles, Calif.

2620 Pollin, William. Control and artifact in psychophysiological research. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 143-155.

When utilizing a control group in psychiatric and psychophysiological research, the assumption that differences between the 2 populations other than the variable we are studying will be randomly distributed between the 2 populations is unwarranted optimism. In order to promote optimum validity, objective personality tests like the MMPI may be used to define the personality characteristics and extent of psychopathology in the control group. Lack of proper attention to such details guarantees a proclivity toward ambiguous results. (21 refs.)

Laboratory of Clinical Science
NIMH
Bethesda, Md.

2621 Handlon, Joseph H. Hormonal activity and individual responses to stresses and easements in everyday living. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 157-170.

A series of studies conducted at NIH on psychoendocrinology dealt with the relationship between the urinary 17-hydroxycorticosteroids and psychological stress. Re-

sponses to normal stress were ascertained by means of the Nowlis-Green Adjective Check List, and quasi-naturalistic studies relied on responses to arousing or bland commercial movies. Hormone levels were also determined with the subject under hypnosis. Initial hospitalization produced an immediate elevation in urinary 17-hydroxycorticosteroids. Modifications in response were also influenced by group background, past experience and the effects of immediate circumstances surrounding admission. (18 refs.)

Department of Psychiatry
Stanford University School of Medicine
Palo Alto, Calif.

2622 Persky, Harold. Adrenocortical function during anxiety. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 171-191.

Bliss determined plasma hydrocortisone levels during anxiety states in a number of patients. Acutely disturbed patients showed a mean hormone level 70% greater than normal subjects. Disruptive anxiety produces the greatest increases in hormone level. Eleven of the 46 steroids which have been isolated from the adrenal cortex have been shown to be true metabolic products of hydrocortisone. The relation between urinary steroid excretion values and tension levels were significantly and negatively related to tension estimates. These findings depend upon increased 17-ketosteroid production or a diminished rate of disposal. Also possible are increased sensitivity to ACTH stimulation or increased corticotropin production. Apparently, emotional arousal leads to adrenocortical activation. (43 refs.)

Indiana University Medical Center
Indianapolis, Ind.

2623 Oken, Donald. The role of defense in psychological stress. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin

Press, 1962, 193-210.

Defenses and related adaptive mechanisms are inextricably bound to the stress response, to the extent that defenses are crucial factors in determining stress responses. Rating scales were developed with full 3 scales; one which deals with the intensity and primivity of defense, a second which separately quantifies defenses operating at the perceptual level and a scale which gauges the extent of adaptive coping behavior. A scale to determine "Situational Cathexis" was also developed. Application of these scales to experimental data provides a far better understanding of the stress reaction. More precise rating scales are badly needed. (11 refs.)

Institute of Psychosomatic and Psychiatric
Research and Training
Michael Reese Hospital and Medical Center
Chicago, Ill.

2624 Graham, David, T. Some research on psychophysiologic specificity and its relation to psychosomatic disease. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 221-238.

In corroboration of the postulated concepts of psychosomatic specificity and psychophysiologic specificity, several studies were carried out to determine the relation between disease and attitude as revealed by initial interviews with hospitalized patients. Attitudinally, the difference between predicted and unpredicted choice responses was significant. Patients with specific diseases were shown a group of cartoons, only 1 of which pertained to a given disease. Verbal choice responses to the cartoons reveal that subjects tend to accept or deny their relevant cartoons, with a difference which corresponds roughly to intelligence level. Some normal subjects were hypnotized and then given attitudinal suggestions compatible with hives, essential hypertension and Raynaud's disease. Results, based upon skin temperature curves, were statistically significant.

University of Wisconsin Medical Center
Madison, Wis.

2625 Roessler, Robert, & Greenfield, Norman S. Incidence of somatic disease in psychiatric patients. In: Roessler, Robert, & Greenfield, Norman S. [Eds.] *Physiological correlates of psychological disorder*. St. Paul: University of Wisconsin Press, 1962. Pp. 257-267.

A comparison of 471 psychiatric patients (average age 21.7 years, with 480 controls (average age 21.4 years, was carried out to test the hypothesis that people with impaired psychological adaptive capacity would demonstrate a greater incidence of somatic disease than controls. Results confirm the hypothesis at appropriate statistical levels of confidence. There is definitely a higher incidence of somatic diseases in those with impaired psychological adaptive capacity rather than mere differential body consciousness between the 2 groups (10 refs.)

Department of Psychiatry
University of Wisconsin Medical Center
Madison, Wis.

2626 Ungar, Georges. *Excitation*. Springfield: Charles C Thomas, 1962. Pp. 1-437.

This monograph covers the development of the excitation concept; living matter and its environment; rest, excitation and recovery; permeability, active transport and adsorption; the biochemistry of excitation; physical processes in excitation; excitation in fertilization and development; receptor and effector systems; communication systems; automatic and rhythmic activity; homeostatic systems; behavior, motivation, learning, memory and consciousness, and the pathology and pharmacology of excitation. Chapters pertinent to psychoactive drugs are summarized in Abstracts Nos. 2627 & 2628. (1253 refs.)

Institute for Comparative Biology
San Diego, Calif.

2627 Ungar, Georges. *Excitation, injury and disease*. In: *Excitation*. Ungar, Georges [Ed.] Springfield: Charles C Thomas, 1962. Pp. 297-323.

the multitudinous ramifications of excitation, injury and disease include inflammation, tissue excitation, phlogogenic stimuli, signs of excitation in inflammation (potassium release, increased glycolysis, histamine release, etc.), capillary permeability, mast cells which release heparin, histamine and 5HT and the role of the nervous system. Extreme stress precipitates shock, or misdirected homeostasis, which constitutes a primary loss of body fluids. (No refs.)

Institute for Comparative Biology
San Diego, Calif.

2628 Ungar, Georges. Excitation and drug action. In: Excitation. Ungar, Georges [Ed.] Springfield: Charles C Thomas, 1962. Pp. 24-353.

Excitation and drug action necessitates the existence of receptors or pharmacoeptive sites. A lengthy dissertation on drug action encompasses the following topics: receptors or pharmacoeptive sites, general cytoplasmic poisons, enzymes as receptors, receptors and ions and receptor proteins. Drugs act by means of cellular excitation, sensory receptors and effectors, synaptic transmission and the CNS. CNS stimulants are subdivided into cortical stimulants (caffeine and amphetamine), convulsants (picrotoxin or pentetrazol), hallucinogens (mescaline, LSD) and excitants with localized effects like tremorine. CNS depressants include barbiturates and mephesisin. Tranquilizers are divisible into 3 main groups: phenothiazine derivatives, Rauwolfia alkaloids and central muscle relaxants. Drugs have been suggested and used, in accord with Huxlian concepts, by mankind for centuries to provide unique pleasures and satisfactions. (No refs.)

Institute for Comparative Biology
San Diego, Calif.

2629 Nebraska State Medical Journal. Thalidomide tragedy could backfire. Nebraska State Medical Journal, 1962, 47, 597; 553. [Editorial]

Apparently Dr. Frances Kelsey's steadfastness which prevented the thalidomide tragedy from striking the American public indicates that present FDA laws are stringent enough to protect the public and they really do not need extensive revamping. Greater cure will undoubtedly be exercised by pharmaceutical companies in the future to preclude any such catastrophe. The Pharmaceutical Manufacturers Association has allocated funds for establishing a Commission on Drug Safety to investigate European problems associated with the thalidomide tragedy. (No refs.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2630 Miller, Ernest C. Functional depression, its recognition and management. Journal of the Louisiana State Medical Society, 1962, 114, 285-290.

The diagnosis of depression must differentiate between normal depression (grief and sadness) and pathologic depression (with insomnia, anorexia, weight loss and vegetative changes). Involutional psychotic reaction also poses a diagnostic problem. Psychotic depressions are best managed with ECT, chlorpromazine and other phenothiazines, hydrazine derivatives (MAO inhibitors), imipramine and trifluopromazine. Dexamphetamine may also be efficacious. Toxicity is frequent with psychoactive drugs. Isocarboxazid (10-20 mg/day), imipramine (25-150 mg/day) and nialamide are also highly recommended. The general practitioner should always feel free to seek outside help when treating a patient with psychotic depression. (13 refs.)

Lake Charles Mental Health Treatment Center
Lake Charles, La.

2631 New Medical Materia. Librium. New Medical Materia, 1962, 4, 60. [Editorial]

Chlordiazepoxide (Librium; 10 mg t.i.d. or q.i.d.) was administered to 29 patients by Brodie and Dow (Portland, Ore.) as an anticonvulsant for 1-18 months. Of the

29, 3 manifested practical seizure control, 3 showed temporary practical control and 13 had a temporary reduction in the number of seizures. Chlordiazepoxide had no effect in 5 patients and 5 became worse. Behavior improved significantly in 2 children with marked mental impairment. Side effects constituted drowsiness or constipation. (1 ref.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2632 New Medical Materia. Ensidon. New Medical Materia, 1962, 4, 60. [Editorial]

Kristof et al. (Montreal, Quebec) administered piperazinoiminostilbene (Ensidon; 150-200 mg/day) to 18 depressed males, aged 37-66 years, for 6-63 days. Results included 10 much improved, 5 improved and 3 relatively unimproved. Ensidon was most efficacious in decreasing depressed effect, sad facial expression, impaired appetite and anxiety, while exerting least effect on apathy, agitation, irritability and decreased sexual interest. (No refs.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2633 New Medical Materia. Quantril. New Medical Materia, 1962, 4, 58. [Editorial]

Benzquinamine (Quantril; 150-1400 mg/day) was administered by Feldman (Topeka, Kan.) to 66 refractory patients (55 schizophrenics, 9 CBS and 2 psychotics with mental deficiency) for an average of 106 days. Significant improvement was shown by 53% of the schizophrenics and 67% of those with CBS. No response was obtained in the 2 mentally retarded patients. Side effects were limited to mild, transient hypotension in 3 patients. (No refs.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2634 New Medical Materia. Sparine. New

Medical Materia, 1962, 4, 58. [Editorial]

Promazine (Sparine; 100 mg-1.2 g/day i.m. or p.o.) was administered by Rolo (Amityville, N.Y.) to 45 patients treated for a stinence syndrome associated with withdrawal of narcotics and barbiturates. Optimal responses were obtained with i.m. administration for 5 days, followed by oral maintenance therapy (75-100 mg/day) for an additional 3 weeks. Promazine induced a state of quiescence bereft of usual tension, restlessness or drug-craving which usually plague the withdrawing addict. No major complications ensued. Epileptic seizures occurred in 5 barbiturate addicts, of whom also had hallucinations and extreme confusion. Pruritis was the only untoward effect. (No refs.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2635 New Medical Materia. Tofranazine. New Medical Materia, 1962, 4, 52. [Editorial]

Pollack (Rochester, N.Y.) administered Tofranazine (25 mg imipramine and 25-50 mg promazine, q.i.d.) to 35 patients (1 schizophrenic and 34 with depressive reactions) for 1-17 months. The 50 mg capsule provided maintenance therapy. More than half the patients received supplementary small nightly doses of chlorpromazine [dosage unspecified], with additional medication at mealtime to control pronounced agitation or anxiety. An overall good clinical response was obtained in 80% with Tofranazine therapy, and anxiety alone was ameliorated in over 90%. (No refs.)

The Hearst Corporation
1790 Broadway
New York 19, N.Y.

2636 Mintz, Stanley R. Drug incompatibilities in anesthesia. Journal of the Louisiana State Medical Society, 1962, 114, 121-123.

The tranquilizers may produce serious reactions when administered in conjunction

th anesthesia. The dicarbamates are not potent enough to allay preoperative apprehension. Dosages of phenothiazine tranquilizers should be minimal since they potentiate the depressant action of barbiturates, opiates and general anesthetics. Chlorpromazine often produces hypotension during anesthesia. The antihypertensives frequently potentiate hypotension during anesthesia. Previous therapy with ACTH or cortisone can result in cardiovascular collapse during anesthetic procedures. Epinephrine predisposes toward development of dangerous ventricular arrhythmias. Cardiovascular collapse may also result from the oxytoxics. Other drugs which induce potentially disastrous side effects include antibiotics, trichlorethylene and anticoagulants. (11 refs.)

Louisiana State Medical Society
New Orleans, La.

2637 Beyer, Karl H. Fetal malformations. *Environmental Health*, 1962, 5, 94-96.

The correlation between thalidomide ingestion during early pregnancy and phocomelia has been unquestionably proven by physicians like Lenz, Knapp, Speirs and Friedemann. The thalidomide tragedy has precipitated an ubiquitous awareness of the need to assess new drug teratogenicity on a preclinical basis. (13 refs.)

Merck Sharp & Dohme Research Laboratories
West Point, Pa.

2638 Baruk, Henri, & Launay, Jacques [Eds.] *Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.* Paris: Presses Universitaires de France, 1962. Pp. 1-390.

This book constitutes an assembly of various papers and original memoirs published in the Cahiers Moreau de Tours or given in the meetings of the Société Moreau-de-Tours, which was established in 1958. This biochemical psychopharmacologic group is made up of clinicians, psychiatrists, pharm-

acologists, physiologists and biologists who meet at Maison Nationales de Charenton, Ecole des Hautes Etudes, Paris. Papers are devoted to the history of psychopharmacology, methods of analysis and reporting, animal psychopharmacology, clinical applications and tests of psychotropic drugs (prochlorperazine, acetopromazine, thioropazine, alimemazine, promazine, imipramine, centrophenoxine, buterophenone derivatives and hydrazines), and neuro-, psycho-, and physiologic, and biochemic studies. Summaries of all papers appear in this issue of Psychopharmacology Abstracts. (85 refs.)

Laboratoire de Psycho-Pathologie Expérimentale
Ecole Pratique des Hautes Etudes
Paris, France

2639 Schuhl, P.M. Les débuts de la psychopharmacologie dans l'antiquité grecque. [The beginnings of psychopharmacology in Greek antiquity.] In: Baruk, Henri, & Launay, Jacques [Eds.] *Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.* Paris: Presses Universitaires de France, 1962. Pp. 3-8.

The use of drugs and psychoactive drugs in Greek antiquity is discussed with particular reference to the Odyssey. The use of various roots and flowers, etc. for the treatment of mental disease, and especially anguish, is elucidated. Mention is also made of Plato's role in pharmacodynamic investigation. (6 refs.)

La Sorbonne
Paris, France

2640 Baruk, H. La vie et l'oeuvre de Moreau de Tours. [The life and work of Moreau de Tours.] In: Baruk, Henri, & Launay, Jacques [Eds.] *Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.* Paris: Presses Universitaires de France, 1962. Pp. 9-14.

Reviews
Abstracts 2641-2643

Joseph Moreau de Tours was born in 1804 and after early education at Ecole de Médecine de Tours became an intern at Charenton in Paris in 1826. His thesis was written in 1830 on delirium, i.e., "monomania." He traveled in the Middle East and studied the effects of marihuana, concluding that its psychotomimetic effects were in some way related to the natural production of delirium. He experimented with marihuana, both on himself and volunteers. This work precedes narcoanalysis, and Moreau de Tours is considered an initiating figure in the development of psychopharmacology. (No refs.)

Laboratoire de Psycho-Pathologie Expérimentale
Ecole Pratique des Hautes Etudes
Paris, France

2641 Collet, C.-G. Candidature de Joseph Moreau (de Tours) au Prix Montyon de l'Académie des Sciences en 1846. [The candidature of Joseph Moreau (de Tours) for the Montyon Prize of the Académie des Sciences in 1846.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 15-21.

In 1846, Moreau presented a paper "Du hachisch et de l'aliénation mentale" to the Académie des Sciences in competition for the Montyon Prize. Marihuana-induced hallucinations were compared to those caused by different opiate preparations, belladonna, alcohol, etc. The germ of the concept of narcoanalysis sprang from the mind of Joseph Moreau from 1837-1845, following his experiences in Egypt and other areas of the Middle East. (1 ref.)

Laboratoire de Psycho-Pathologie Expérimentale
Ecole Pratique des Hautes Etudes
Paris, France

2642 Baruk, H. L'expertise et les décrets récents en psychopharmacologie. [Report

and recent decrees in psychopharmacology.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 25-28.

The use of a range of laboratory animal with emphasis on monkeys, in the testing of psychoactive drugs is underlined. Some tests used are: potentiation of narcotics and analgesia; hypothermia; antiseroton activity in vitro; the traction test; the Winter and Flataker test; CR tests; antapomorphine activity, and in the pigeon the ground perception test. In man clinical trials encompass subjective modifications in mentation, study of the psychomotor curve combined with study of fatigue, ECG, hematograms, sedimentation rate, labyrinth reactions, standard laboratory tests, hormone assay, etc. The tightening of drug regulations in France following "la catastrophe du Stalinon" (the thalidomide tragedy), with reference to Art. 5120-2 of the Code de la Santé Publique is elucidated. (3 refs.)

Laboratoire de Psycho-Pathologie Expérimentale
Ecole Pratique des Hautes Etudes
Paris, France

2643 Launay, J. L'expertise psychopharmacologique. Expérimentation animale, essais cliniques. [Psychopharmacologic report. Animal experimentation and clinical trials.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 29-31.

The division of psychopharmacologic experimentation into toxicology, pharmacology and chemistry is outlined. Drugs should be tested in increasing doses in a variety of laboratory animals. In the clinic psychomotor activity is usefully measured by the Mosso ergograph; laboratory tests are found essential and with some drug treat-

electrolytes and hormones are also assayed. (No refs.)

Hôpitaux Psychiatrique
Paris, France

2644 Borenstein, P., & Dabbah, M. Utilité du contrôle E.E.G. des drogues psychotropes. [The utility of EEG control of psychotropic drugs.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 32-34.

EEG's are made before, 30 and 60 minutes after and 24 hours after the administration of a psychoactive drug. Epileptogenic activity, diffuse or localized disturbance, marked modifications in frequency, amplitude, etc., judgements on the drug excretion based on modifications of the EEG and the total absence of EEG modification put in doubt CNS action due to the psychoactive drug. Correlation between clinical and EEG results is still a topic of controversy. (No refs.)

Hôpitaux Psychiatrique
Paris, France

2645 Leyritz, J. Tests biologiques concernant les médicaments psychotropes. [Biological tests for psychotropic drugs.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 35-38.

This discussion centers on drug effects on cerebral catecholamines and enzymatic action (MAO and COMT). The necessity of research on causative factors in psychopathologic disorders is stressed. Two proposals are made directed to the Santé Publique (France): the creation of a pharmacological research center which would fix routes of administration, dosage, describe side effects in both the CNS and

general system (particularly hepatic and renal functions), and publish observations on biological tests and assay methods; endow sufficiently qualified psychiatric hospitals with the means of following their patients with all the resources of modern medicine. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2646 Coirault, R. Les examens biologiques et l'expertise des drogues psychotropes. [Biological examinations and report on psychotropic drugs.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 39-42.

The difficulties inherent in extensive biological testing of mental patients under drug therapy are outlined. Aside from common laboratory tests, variations in electrolytes, enzymatic variations, oxidases, transaminases, dehydrogenases, etc. catecholamine assays and changes in hormone excretion, as well as bioelectric tests (neuromuscular excitability, electromyography, study of the myotactic reflex, ECG and EEG, etc.) should be followed. Difficulties in interpretation, e.g., the meaning of a hypopotassemia, are also elucidated. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2647 Baruk, H., Launay, J., & Perlès, R. Les phénothiazines et la psychiatrie. [Phenothiazines in psychiatry.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 45-62.

The chemical structure of phenothiazine

and relationships to animal experimentation are reviewed. Potentiation of narcosis and analgesia, hypothermia, antiserotonin activity in vitro, the traction test, the Winter and Flataker test, tests for CR's, anti-apomorphine activity and catalepsy, experimental catatonia, and the deJong and Baruk test are emphasized. Psychomotor, ergographic and ECG modifications, as well as those in other bioelectrical tests are outlined. Information is presented on chlorpromazine, prochlorperazine, thiopropazine, levomepromazine, acetomepromazine and alimemazine, with emphasis on work in monkeys. Classification scheme of Decourt and that of Courvoisier, Lambert and Revol is presented along with Baruk and Launay's scheme. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2648 Courvoisier, S., & Lambert, P.-A. Essai de classification pharmacologique et clinique de certains neuroleptiques à structure phénothiazinique. [Pharmacologic and clinical classification of some phenothiazine neuroleptics.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 63-72.

The sedative, depressive, antiapomorphinic and cataleptic qualities of chlorpromazine, methopromazine, alimemazine, levomepromazine, prochlorperazine, thioperazine, promazine and acepromazine are reviewed. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2649 Courvoisier, S. Expérimentation animale de la prochlorperazine. [Animal experimentation and prochlorperazine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours.

Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 73-74; discussion 74.

The sedative, depressive and antiemetic properties of prochlorperazine and chlorpromazine are compared. The sedative and depressive characteristics of prochlorperazine are markedly less than those of chlorpromazine, while its antiapomorphine antagonism is 4-5 times greater than that of chlorpromazine. Experimentation with monkeys is emphasized. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2650 Baruk, H., & Launay, J. Résultats de l'expérimentation de la prochlorperazine sur le comportement du Singe. [The results of experimentation with prochlorperazine on behavior in the monkey.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 75-78.

Nine monkeys were given 0.5-33 mg/kg prochlorperazine. At high doses catatonia was observed and at low doses bizarre attitudes approaching hysteriform manifestations. At a still lower dose cataleptic sleep was observed, not seen with other phenothiazines, and at a very low dose psychomotor excitation with lack of coordination. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2651 Baruk, H. Notre expérience des effets thérapeutiques du tartrate d'alimemazine. [Our experience with the therapeutic effects of alimemazine tartrate.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- An

als of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. p. 122-123.

climemazine, of moderate hypnotic activity, an excellent substitute for barbiturates, is recommended. However in about 5% of cases, nightmares and nocturnal onerisms are observed. Also it can be used in combination with imipramine in order to reduce the exciting properties of the latter. Climemazine has not demonstrated any epileptogenic properties or "neuroleptic" (i.e., extrapyramidal syndrome inducing) properties. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2652 Cahn, Th. Machines électroniques et fonction nerveuse supérieure. [Electronic machines and higher nervous function.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 291-293.

Computers are compared in function to cerebral functions, with mention of the electronic roles of condensers, oscillators, etc. The heterogeneity and complexity of the CNS and its interconnections are stressed. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2653 Cahn, Th. La structure de l'espace et la structure de l'organisme. [Structure of space and form of the organism.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 295-298.

Emotion, mentation, will, human expression through writing and speaking, Platonic versus Aristotelian concepts of space, perception and sensory organs, and underlying mechanisms are expounded. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2654 Cahn, Th., & Houget, J. Mise en évidence de la défense de l'organisme dans la réponse à de faibles quantités d'hormones. Généralités possibles de ce processus. [Evidence of body defenses in response to low amounts of hormones. Possible properties of this process.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 299-302.

Constitutional genetic differences in relation to responses to hormone administration is reviewed, e.g., the variation in glycemia from 1 species to another in response to epinephrine or insulin. The work of Claude Bernard and followers is elucidated. The heterogeneity of the body and equilibrium system, with reference to Le Chatelier's equilibrium principle, are noted. The role of pharmacological agents in displacing equilibria is commented on and the necessity for judicious analysis on the eventual role of a drug is stressed. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2655 Cahn, Th. Modèles électroniques et fonctionnement de l'organisme. [Electronic models and the functioning of the body.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 303-308.

Reviews
Abstracts 2656-2659

The regulation of metabolic reactions is compared to the activity of electronic machines. The great differences between organ activity and activity on the molecular level are stressed. Memory and the problem of inscription in relation to CNS liaisons are noted in reference to computer construction. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2656 Cahn, Th. Sur la pensée et ses connexions avec l'organismes. [On thinking and its connections in the system.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 309-315.

The inherent independence of human thought allows analysis of the events in the environment. The fragility of cerebral function as indicated by intoxication, damage from fever or diseases is evident. Dialects, language and logic and their development from Plato through Descartes to the present are outlined. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2657 Cahn, Th. Sur l'activité métabolique des organismes. [On the metabolic activities of organisms.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 316-321.

The role of biology as a science in the theoretical and practical examination of metabolism is discussed. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2658 Cahn, Th. Sur la méthode en biologie. [On method in biology.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 322-323.

The extreme heterogeneity of macroscopic and microscopic biological systems is treated historically. The difficulties of transposing information obtained in animal experimentation to clinical medicine is briefly noted. (No refs.)

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2659 Georgi, F. Ethiopie, ancienne culture immobilisée et invasion de la civilisation. [Ethiopia, static ancient culture and the invasion of civilization.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 381-385.

Medical details are given on impoverished, syphilis-ridden, malaria-ridden Ethiopia. It is difficult for outside medical specialists to attempt to provide aid to this country of 20 million people where only 4% of the national budget is spent in public health. (No refs.)

Department de Neurologie
Université de Bâle
Basel, Switzerland

See also 2687, 2751, 2754

CLINICAL STUDIES

2660 Hunt, G. Halsey, & Odoroff, Maurice E. Followup study of narcotic drug addicts after hospitalization. Public Health Reports, 1962, 77, 41-54.

Of 1,912 narcotic addicts in N.Y. City who were discharged from the USPHS Hospital at Lexington, Ky., between July 1952 and December 1955, 90% became readdicted, and more than 90% of those who became readdicted did so within 6 months after discharge. Age provided a significant variable, with men over 30 years of age having generally lower readdiction rates than those under 30. In addition, significantly lower readdiction rates were found for nonvoluntary patients over 30 years of age, white, nonvoluntary patients aged less than 30 years and patients under 30 years hospitalized for more than 31 days.

Division of General Medical Sciences
NIH
Bethesda, Md.

2661 Rackow, Herbert, & Salanitro, Ernest. A dose-effect study of preoperative medication in children. Anesthesiology, 1962, 23, 747-754.

Dose-effect relationships were established on a double-blind basis with secobarbital (0.5-2.0 mg/lb i.m.), morphine (0.5-.15 mg/lb i.m.) and pethidine (0.5-1.5 mg per lb i.m.) or a combination thereof, in 1791 children all who were apprehensive, calm and wakeful or sleepy 1 hour before surgery. All 3 drugs showed similar efficacy in reducing apprehension. Secobarbital, however, was 4 times as effective as morphine or pethidine in increasing the incidence of sleeping children. A combination of secobarbital and morphine was more effective than either drug alone in reducing the incidence of apprehension and sleeping children. Combinations of secobarbital and pethidine failed to produce this effect.

Department of Anesthesiology
College of Physicians and Surgeons
Columbia University
New York, N.Y.

2662 Binning, Rex, Watson, W.R., Samra, M., & Martin, Esmee. Premedication for adenotonsillectomy. British Journal of Anaesthesiology, 1962, 34, 812-816.

A total of 121 children aged 2½-8 years, received quinalbarbital (6 mg/kg), 120 received promethazine and chlorpromazine (0.8 mg/kg each), 135 received trimeprazine (4 mg/kg) and 80 received atropine (0.9 mg/kg) on a double-blind basis as premedication for adenotonsillectomy. Atropine (0.9 mg) was administered p.o. to all patients to dry up secretions. Preoperative vomiting occurred in 47%. Two-thirds of the quinalbarbital treated patients were asleep on arrival in the anaesthetic room, and 57% vomiting occurred postoperatively. With promethazine and chlorpromazine, only 25% of the children were asleep at the time of induction, and 36% postoperative vomiting ensued. With trimeprazine, 2/3rds of the patients were awake during induction. Trimeprazine is the most efficacious premedication to date available for younger children facing an inhalational induction.

Royal Alexandra Hospital for Sick Children
Brighton, Great Britain

2663 Cross, Thomas N. A ten-year study of the inpatient population of the adult psychiatric service. University of Michigan Medical Bulletin, 1962, 28, 37-40.

From 1950-1960, 3 samplings of data culled from the Adult Service of the Neuropsychiatric Institute of the University of Michigan Medical Center reveal a progressive increase in the number of emergency admissions and of patients with more serious illnesses. In 1950, 21 patients received ECT while only 2 received ECT in 1960. In 1960, of 89 patients receiving tranquilizers or antidepressants, 73 were treated with phenothiazine derivatives or similar drugs and 16 took antidepressants. Inpatient populations tend toward fewer patients with neuroses and more with psychoses, necessitating profound alterations in treatment, teaching and research activities.

Department of Psychiatry
University of Michigan Medical Center
Ann Arbor, Mich.

2664 Munson, Wayne M., & Jenicek, John A. Effect of anesthetic agents on patients receiving reserpine therapy. *Anesthesiology*, 1962, **23**, 741-746.

A total of 58 patients received reserpine (1-5 mg parenterally) to determine drug effects on response to anesthesia. Therapy was maintained in 42 until 5 days before surgery. In the control series, 16 were withdrawn from therapy within 8 days of surgery. Neurocirculatory instability was demonstrated by 9 out of 16 in a previous series, 13 out of 26 in the present series and 7 out of 16 in the control series. The control series revealed no significant decrease in the incidence of severity of hypotension during induction of anesthesia. Rauwolfia derivatives need not be discontinued before anesthesia and surgery, as drug withdrawal does not insure prevention of circulatory stability

Anesthesia and Operative Service
Brooke General Hospital
Brooke Army Medical Center
Fort Sam Houston, Tex.

2665 Hankoff, Leon D. Treatment comparison and the placebo effect. *Diseases of the Nervous System*, 1962, **23**, 39-40.

Positive placebo responses were observed in a hospitalized 29-year-old woman with apathy, confusion and tenseness. A 34-year-old man with recurrent uncontrolled bizarre thoughts received meprobamate (200 mg as needed), thiopropazate (5 mg t.i.d.) and chlordiazepoxide (50 mg t.i.d.) for varying periods of time. Considerable improvement was observed with chlordiazepoxide. A 43-year-old woman with acute delusional episodes responded well to a daily regimen of meprobamate (400 mg b.i.d.), pyribenzamine (50 mg t.i.d.) and a belladonna-barbiturate mixture t.i.d. Substitution of placebos for meprobamate resulted in subjective feelings of dizziness, nausea, blindness and numbness around the mouth. An inert or active psychopharmacological a-

gent may precipitate a variety of responses depending upon clinical conditions and other factors.

Department of Psychiatry
State University of New York
Downstate Medical Center
Brooklyn, N.Y.

2666 Yi-Yunh Hsia, David, Rowley, William, & Raskin, Nathaniel J. Clinical management of phenylketonuria. *Quarterly Bulletin of Northwestern University Medical School*, 1962, **36**, 25-32.

A low-phenylalanine diet was administered to 12 phenylketonurics, below 3 years of age at initial diagnosis in order to prevent or minimize mental retardation. The diet was maintained for 324 months, and good biochemical control was sustained. Four of the 5 children who began the diet before the age of 6 months are normal intellectually. In contrast, 6 out of 7 whose diet began after 1 year of age are retarded. A general increase was observed in intellectual growth rate among the 6 who were retested. Mental deficiency can be prevented or controlled by institution of a low-phenylalanine diet before age 6 months. A national program is in progress to screen newborn infants for phenylketonuria at 3-4 weeks of age.

Department of Pediatrics and Neurology
and Psychiatry
Northwestern University Medical School
Evanston, Ill.

2667 Powell, L.W., & Schonell, M.E. The role of bemigrade in the treatment of barbiturate overdosage: results of a controlled study. *Medical Journal of Australia*, 1962, **1**, 551-552.

Bemigrade (1 g i.v.) or saline was administered to 102 patients, average age 39.9-40.8 years, presented with barbiturate overdosage (greater than 50 grains). Mephentermine or albumin was given to raise blood pressure. Physicians recorded level of consciousness, pupillary and tendon reflexes, pulse rate, blood pressure and respiratory rate. Only 1 death occurred. Re-

sults indicate that albeit bemegride may diminish the time required for an unconscious patient suffering from an overdose of barbiturate drugs to respond to painful stimuli, it does not alter the time taken for such patients to reach a satisfactory safe stage. Results confirm the original hypothesis that bemegride is of no significant value in alleviating barbiturate overdosage.

Brisbane Hospital
Brisbane, Australia

2668 Figurelli, Francesco A., Davis, Robert, & Figurelli, Jean. Severe and complicated delirium tremens: result of promazine therapy in a selected group. *Medical Times*, 1962, 90, 1347-1353.

Promazine (100-200 mg i.m., followed by 50-200 mg q.i.d., p.o.) was administered to 195 patients, average age 46 years, with severe delirium tremens. Supportive therapy in select cases included antibiotics, vitamins, meprobamate, promethazine, prochlorperazine and reserpine, etc. Standard laboratory tests followed admission. Analysis for morbidity and mortality revealed that 24 patients or 12% died. Of the remainder, 27 had pulmonary infections, 39 had liver damage and 18 had multiple complications. A combination of delirium tremens, pulmonary infection and liver damage produced the highest morbidity. With promazine, the mean duration of delirium was only 6 days. Side effects included hypotension in 5 and toxicity in 1.

Seton Hall College of Medicine
Jersey City, N.J.

2669 Whittemore, J.B. A clinical and experimental study of bromide intoxication, with special reference to bromureides. *Medical Journal of Australia*, 1962, 1, 422. [Letter]

For the type of patient who feels he's run down, irritable, etc. with no physical illness mixtures containing 10 grains potassium bromide and 1/4 grain sodium phenobarbital t.i.d. with appropriate symptomatic treatment for accompanying complaints

such as anorexia, flatulence or insomnia, is recommended. This had 2 advantages over most of the tranquilizers, hypnotics, etc.: it is inexpensive and never causes stuffy nose, dry throat or thirst.

112 Willison Road
Carlton, New South Wales
Australia

2670 Alexander, Daniel D. Observations in the use of Tindal. *Diseases of the Nervous System*, 1962, 24, 351.

Fifty-six patients, 49 women and 7 men, were treated with acetophenazine (Tindal). Fifty of the patients were 50-95 years of age and 22 of these were 70-80. Twenty-six had organic brain disease. The majority took 20 mg acetophenazine t.i.d., and a few took 20 mg t.i.d. or only once. Sixty-eight percent showed definite improvement, 25% did not change and 7% were not as well as when they had been treated with other drugs. The greatest improvement was observed in psychomotor activity; 31 overactive patients then became noticeably quieter. Improvements were noted in personal appearance, social relationships, clearer speech, etc. The mood of 10 depressed patients became elevated, although 2 others showed no change. The only adverse hematological reaction was leukopenia in 1 patient. Five patients complained of drowsiness and 1 instance of drooling was noted.

Danvers State Hospital
Hathorne, Mass.

2671 Cohen, Harry. Treatment of chronic regressive refractory schizophrenia. *Diseases of the Nervous System*, 1962, 24, 335-339.

Hydroxyzine (100-500 mg t.i.d., p.o.) was administered to 40 chronic refractory female schizophrenics, aged 23-70 years, for 10-12 weeks. Minimal improvement was observed in 12.5%, indicating that hydroxyzine is not particularly suited for severely regressed, poorly motivated patients. Side effects occurred in 95%, including ataxia, restlessness, tremor, grand

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mal seizures, drowsiness, etc. At the most economic therapeutic dosage level, however, there were few side effects.

Brooklyn State Hospital
Brooklyn, N.Y.

2672 Clarke, Edward T. Observations on Benizol therapy in general practice. Ninety senile patients. Medical Record and Annals, 1962, 55, 186-189.

Ninety senile or arteriosclerotic cases (47 ambulatory), aged 56-93 years and averaging 77 years, were treated for 12 weeks with Benizol (100 mg pentetrazol and 50 mg nicotinic acid). Dosage varied from 1 or 2 tablets or teaspoonsful t.i.d. Improvement percentages were: appearance 77, personal habits 74, physical condition 91, sociability 76, depression 74, feeling 95, memory 79, work habits 63, eating habits 71 and sleep patterns 80. Twenty cases were not so tabulated and were clinically rated: 14 very good, 5 good and 1 no improvement. Slight flushing of the skin in some patients due to nicotinic acid was the only side effect; in 4 cases with high blood pressure some slight change towards normal was recorded.

3801 Kirby Drive
Houston, Tex.

2673 Dorfman, Wilfred, A short-acting anaesthetic in psychiatry. Diseases of the Nervous System, 1962, 23, 276-278.

Methohexital (8-10 cc of 1% solution i.v.) was administered to 75 patients before ECT, for a total of 650 injections over a 14-month period. In addition, 38 patients received methohexital as a method of narcoanalysis. With methohexital, the patient recovered completely within 15-30 minutes. In narcoanalysis, patients emerge from anesthesia in a more receptive state. Rapid symptom removal was frequently accomplished for psychosomatic symptoms under methohexital narcoanalysis.

1921 Newkirk Avenue
Brooklyn 26, N.Y.

2674 Davies, D.L. Normal drinking in recovered alcohol addicts. Quarterly Journal of Studies on Alcohol, 1962, 23, 94-104.

Seven male alcoholics, aged 26-47 years, were treated with disulfiram and psychotherapy for 2-5 months and discharged. Follow-up studies revealed that they had subsequently been drinking socially for 7-11 years after their discharge without getting drunk. All were better socially adjusted than they had been 1 year before admission. Apparently the old maxim that no reformed alcoholic is capable of normal drinking should be revised.

Professional Unit
Maudsley Hospital
London, Great Britain

2675 Pommé, B., Blanche, R., Girard, J., & Yermia, H. Utilisation du librium en psychiatrie (forme orale et injectable). [Use of Librium in psychiatry; (oral and injectable form).] Annales Médico-Psychologiques, 1962, 120, 1, 146.

Chlordiazepoxide (Librium) had marked tranquilizing activity in neurotic and anxiety states, neuroses with psychosomatic manifestations, post-epileptic syndromes and post-traumatic neuroses, as well as acute alcoholic deliriums [no details]. The drug was used only at doses of 40-400 mg per day, or in combination with a thymoanaleptic.

[No address]

2676 Fourny, M., Combette, M., Stéphanopoli, M., & Ségal, M. Evolution du traitement des accidents aigus de l'alcoolisme chronique: utilisation de l'halopéridol comme médication de base. [The course of the treatment of acute incidents in chronic alcoholism: use of haloperidol as a basic medication.] Annales Médico-Psychologiques, 1962, 120, 1, 146.

Fifty cases of acute incidents (delirium tremens, etc.) in chronic alcoholism were treated with haloperidol i.v. [dosage unspecified] and then p.o., combined with i.m. chlorpromazine. Haloperidol was found

life and allowed rehydration of the patient p.o. This treatment did not require the strict surveillance necessary when anti-motor agitation drugs are used.

No address]

2677 Ackner, Brian, Cooper, J.E., Gray, J.H., & Kelly, Margaret. Acute porphyria: neuropsychiatric and biochemical study. *Journal of Psychosomatic Research*, 1962, 1, 1-24.

Thirteen patients, aged 20-61 years, with acute porphyria were subjected to psychiatric, psychological and EEG investigations, together with daily measurement of the urinary excretion of porphobilinogen and δ -aminolevulinic acid. No evidence was obtained to indicate a psychogenic factor in the etiology of the disorder or a neurotic predisposition in family history or previous personality. Excretion of porphobilinogen and δ -aminolevulinic acid fluctuated considerably but there was no correlation between peaks of excretion and acute symptoms. Psychiatric symptoms occur commonly during an acute attack of porphyria.

St. Bartholomew's Royal Hospital
London S.E.5, Great Britain

2678 Clout, I.R. Neurosis in general practice. A therapeutic study. *Medical World*, 1962, 96, 383-386.

Parstelin (10 mg tranylcypromine and 1 mg trifluoperazine), was administered p.o., i.d. to 115 patients, aged 30-55 years, with anxiety, tension and depressive states for an average of 7 weeks. Results were excellent in 41, much improved in 38, improved in 16 and unimproved in 20. Remarkable improvement was observed in patients with chronic impotence. In toto, 88.7% recovered and 13% were partially improved. Few serious side effects were observed. Superficial psychotherapy was conducted concomitantly. There was no risk of suicide or addiction. Parstelin is highly recommended for safe, effective emergency treatment of psychiatric patients in general practice.

No address]

2679 Collard, J., & Kerf, J. Le traitement de l'anxiété névrotique par le valium. [Treatment of neurotic anxiety with Valium.] *Encéphale*, 1962, 51, 571-573.

Eighteen cases of psychoneurotic depression, 5 cases of anxiety, 4 of obsessional neurosis and 1 conversion reaction (total 28) were treated with an optimal average of 15 mg/day diazepam (Valium) in 3 divided doses. Two were cured, 5 markedly improved, 14 showed improvement and 8 slight improvement with no failures. The side effects were drowsiness in 22% and some slight euphoria.

Clinique Psychiatrique
Université de Liège
Liège, Belgium

2680 Langston, William B., Jr. Psychotic and psychoneurotic states. Treatment with chlordiazepoxide. *Southwestern Medicine*, 1962, 43, 295-298.

Chlordiazepoxide (10-75 mg/day) was administered to 130 psychiatric patients aged 16-75 years, with a variety of psychotic and psychoneurotic disorders. Dosage was usually 10 mg, 2, 3 or 4 times daily and the duration of treatment was from 1 day to 5 months. Seventy patients received adjunctive therapy with iproniazid, mescopalamine, isocarboxazid, glutethimide and chlorpromazine. Responses were excellent in 22.2%, good in 38.1% and fair in 11.1%. Thirty-six percent showed no improvement. In anxiety reaction 8 out of 12 had excellent response, while in depression only 5 out of 44 had an equivalent response. Side effects were infrequent; ataxia was observed in 6 patients, drowsiness in 8 and one patient developed a skin rash. It was necessary to discontinue medication in only 2 patients.

703 North 6th St.
Longview, Tex.

2681 Caldwell, William G. The treatment of premenstrual tension and dysmenorrhea with a non-narcotic analgesic. *Southwestern Medicine*, 1962, 43, 68-74.

A 128 cases of premenstrual tension (abdominal water retention 121, headaches

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93, etc.) and 248 cases of dysmenorrhea (severe cramps 227, low back pain 172, etc.), aged 16-48 years, were treated with Fiorinal (50 mg butalbital, 200 mg acetylsalicylic acid, 40 mg caffeine and 130 mg phenacetin). Forty-two cases had pelvic pathology and 21 of these received surgical treatment. Fifty-three patients suffered from both premenstrual tension and dysmenorrhea. One-hundred and fifty-four were unmarried, 94 married, 51 having borne 1 or more children. An initial dose of 2 Fiorinal tablets taken at the 1st sign of symptoms, followed at 4 hour intervals with 1 or 2 tablets, proved the most efficient dosage schedule. Dosage requirements were 1-12 tablets given over a 2 day period; the overall average dosage was 4-6 tablets. Individualization permitted a reduction of dosage in 137 cases. No side effects were noted in any of the patients. One-hundred and ninety-four cases whose symptoms varied from very severe to moderate obtained excellent to good results.

Department of Clinical Research
St. Anne's Hospital
Los Angeles, Calif.

2682 Guyotat, J., & Hochmann, J. Situation actuelle du 8228 R.P. en thérapeutique psychiatrique. Apropos de 32 nouveaux cas. [The present position of RP 8228 in psychiatric therapy; on 32 new cases.] *Lyon Médicale*, 1962, 43, 777-783.

Levophacetoperazine (RP 8228; 5-10 mg/day p.o.) was used in the treatment of 32 adults, 21 ambulatory and 11 hospitalized. Among ambulatory patients, 5 had excellent results, 1 an average result and the rest were dropouts, cured of either their ailment or their doctor. Among the hospitalized group excellent results were obtained in 2 (asthenia and exhaustion neurosis) and good results in 8. One failure, depression in an Algerian immigrant, was recorded. After eliminating dropouts, excellent results were obtained in 40%, good results in 50% and failure in 10% of the remaining 18 patients.

Clinique Neuro-Psychiatrique et d'Hygiène Mentale
Université de Lyon
Lyon, France

2683 Delay, J., Deniker, P., & Benoit, J.C. Evolution psychosomatique d'une lombalgie. [The psychosomatic course of a case of low back pain. Combination chemotherapy and psychotherapy.] *Acta Psychotherapeutica et Psychosomatica*, 1962, 10, 76.

A case of low back pain with sciatica complicated by psychiatric factors, including affective immaturity, homosexuality and hypochondriac preoccupation is described which improved markedly on iproniazid [dosage unspecified].

[No address]

2684 Jensen, Sven E. A treatment program for alcoholics in a mental hospital. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 315-320.

A program which included group and work therapy, discussions and individual psychotherapy, and LSD therapy, was followed by 58 alcoholics who were subsequently studied for 6-18 months. Towards the end of hospitalization (average 2 months) 200 γ LSD is administered and conflict material carefully gone over with the patient. Sometimes 2 or 3 sessions are needed because of overwhelming anxiety in the 1st. Of these, 38 remained totally abstinent, 7 improved, 13 were unimproved and 7 were lost to followup. An additional 35 patients received the same treatment without LSD, and 4 were abstinent, 4 improved, 9 unimproved and 18 lost. Individual psychotherapy administered to 45 controls resulted in 7 abstinent, 3 improved, 12 unimproved and 23 lost.

[No address]

2685 Stevens, John D. Dual function of psychotherapeutic antihistamine (tranquili-zer-antiallergic) in schizophrenia. *Diseases of the Nervous System*, 1962, 23, 416-418.

Tripeleennamine (100-200 mg t.i.d.) was administered to 26 phenothiazine-sensitized schizophrenics with allergic conditions. Of the 4 who found phenothiazines intolerable, 2 exhibited excellent responses to tripeleennamine and 2 became more placid. Phenothiazines became tolerable to 19 patients when tripeleennamine was adminis-

ered concomitantly, and 3 other patients subsequently were observed. Antihistamines may be useful adjuncts for such problems in combination with tranquilizers.

VA Hospital
Sepulveda, Calif.

2686 Keats, Sidney, Kambin, Parviz, & Nordlund, Thora. Use of a new relaxant drug in cerebral palsy. *Diseases of the Nervous System*, 1962, 23, 399-403.

Chlordiazepoxide (5-40 mg/day) was administered to 72 children with cerebral palsy with spasticity, rigidity, ataxia flaccidity and athetosis, aged 3-17 years, for an average of 4.3 months. On the basis of absence of side effects coupled with improved physical and emotional status, 41 showed good to fair responses, 35 were unchanged and 10 responded poorly. Spastic patients exhibited the most improvement. Aside from its muscle relaxing effect, it was beneficial in concomitant anxiety and tension.

Cerebral Palsy Clinic and Treatment Center
New Jersey Orthopedic Hospital
Hospital Center
Orange, N.J.

2687 Bonnet, H. Psychosenbehandlung mit modernen Pharmaka. Bedeutung bestimmter Kombinationen. [Treatment of psychoses with modern pharmacologic agents. The importance of certain drug combinations.] *Medicina Experimentalis*, 1962, Suppl., 7, 5-86.

The treatment of psychosis is discussed in very general terms. The combination of prochlorperazine (20-100 mg) and levomepromazine (35-250 mg) improved 15 out of 66 schizophrenics and in chronic delirious patients with hallucinations. The combination imipramine, meprobamate and methylphenotholcarbamate produced excellent results in 56 of 62 ambulatory patients [no diagnosis, and no dosage specified]. Tranquilizing or neuroleptic drugs together with sedatives [not specified] are recommended for insomnia.

Hôpital Psychiatrique Sainte-Marie
Montredon, Le Puy (Haute-Loire), France

2688 Rabe, F., Penin, H., & Matthes, A. Erfahrungen mit Ospolot in der Epilepsiebehandlung. [Some experiences with Ospolot in the treatment of epilepsy.] *Deutsche Medizinische Wochenschrift*, 1962, 87, 953-959.

Ospolot is a sulfonamide derivative (N-(4'-sulfamyl-phenyl)-butansultam-(1-4)). Two hundred and thirteen patients (47 children under 14 years of age) with psychomotor attacks with or without grand mal seizures were treated; with few exceptions observations were continued for at least 6 months. Dosage: for children $1\frac{1}{2}$ -5, adults 2-15 tablets daily (mostly $\frac{1}{2}$ -3, and 4-6, respectively) [amount unspecified]. Of 57 patients with isolated psychomotor attacks 10% remained free of attacks and 30% were improved; 53% could not be improved and in 7% the attacks occurred more frequently. The treatment was even less effective in 89 cases of combined psychomotor attacks and grand mal. The effect of Ospolot on the minor attacks of petit mal, Jacksonian epilepsy, or adverse or cortical epilepsy (29 cases) was not significant. Sixteen percent of 40 patients with grand mal epilepsy could be relieved of attacks; a result which is clearly inferior to that of other antiepileptic agents. Side effects were noted in 75% of the patients: paresthesia in 38%, tachypnea and hyperpnea in 30%, cardiovascular symptoms in 7%, and gastrointestinal symptoms in 14%. Loss of weight was seen in 8% and various functional disturbances in 24%. For these reasons, Ospolot is contraindicated for persons with vasomotor lability, with hyperthyroidism or arterial hypertonia. In 14% of the patients the treatment resulted in abnormal excitation. Due to the insignificant anti-epileptic effect, and the high percentage of side effects, Ospolot is not recommended as treatment of choice for psychomotor attacks or grand mal seizures. Under certain conditions, however, it is useful as an adjuvant.

Nervenklinik der Universität Heidelberg
Heidelberg, Germany

2689 Tölle, Rainer. Über zwei Piperazinderivate des Phenothiazins. [Two piperazine phenothiazine derivatives.] *Nervenarzt*, 1962, 10, 457-462.

Twenty-nine acute and chronic schizophrenics, 19-55 years of age, were treated

with prochlorperazine (60 to 120-200 mg/day/p.o.). The results were excellent in 6 cases, good in 6 and questionable in 4. Improvement did not seem to depend on dosage and appeared usually within the 1st 3 days of treatment. Side effects were seen in 62% of the patients; dyskinetic and hyperkinetic symptoms appeared most often within the 1st 3 days, psychic disturbances similar to Korsakow's syndrome after 3-4 weeks. Thirty-six schizophrenics, mostly acute cases, received thioproperazine (30-90 mg i.m. daily during the 1st 3 days, later 60-140 mg/day/p.o.). Therapeutic results were favorable; side effects similar to those experienced with prochlorperazine occurred in 48% of the patients. The side effects could greatly be reduced by simultaneous administration of beperidene. Patients with severe schizophrenic defects showed the poorest response.

Privatklinik Christophsbad
Göppingen, Germany

2690 Wachsmuth, R. Fluphenazin - mehr als ein neues Psychopharmakon. [Fluphenazine - more than a new psychopharmakon.] *Nervenarzt*, 1962, 10, 466-469.

One-hundred and sixty-one hospitalized patients treated with fluphenazine were investigated in regard to over-all clinical effect and drug influence on target symptoms examined. The medium standard dosage was 3-6 mg/day p.o. or i.m.; no patient was treated less than 4 weeks. The patients suffered from schizophrenia, hebephrenia, catatonia and paranoia. The average age was 33-41 years and 124 subjects were men. The drug was generally well tolerated; it is compatible with barbiturates and antidepressants and ECT. Effects were very good in 68 patients, good in 50, moderate in 20 and uncertain in 14. No effect was noted in 9 patients. There were no toxic or cardiovascular side effects. Overdosage leads to extrapyramidal symptoms; i.m. administration not infrequently leads to hyperkinetic-dystonic syndrome.

Westfälische Landeskrankenhaus
Gütersloh, Germany

2691 Jonsson, Carl-Otto, Cronholm, Börje, & Izikowitz, Sander. Intellectual changes in alcoholics. Psychometric studies on mental sequels of prolonged intensive abuse of alcohol. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 221-242.

Thirty recently hospitalized male alcoholics, 30 previously hospitalized alcoholics and 29 controls, mean age 45 years, with widespread nonpsychotic mental disturbances received the following tests to determine intellectual performance: 5 tests of verbal understanding, 1 each of verbal fluency and reasoning ability, 2 tests of spatial thinking, 3 of memory, 3 digit symbol tests and various subtests of the Wechsler-Bellevue Scale and Grassi's test. Most test revealed that results were greatly improved among alcoholics at the termination of hospitalization. Apparently, a partially reversible impairment of intellectual ability exists immediately after a period of intensive alcohol abuse. Memory impairments are significantly ameliorated by hospitalization.

Beckomberge Sjukhus
Bromma 4, Sweden

2692 Aivazian, G.H. Amitriptyline in the treatment of depressive states. *Diseases of the Nervous System*, 1962, 23, 410-415.

Amitriptyline (75-300 mg/day p.o. or 10-20 mg t.i.d. or q.i.d. i.m.) was administered to 52 hospitalized depressed patients (36 with depressive reaction, 5 CBS and 11 depressed schizophrenics), aged 17-72 years, for 3-10 months. Combined chemotherapy was utilized in 14 patients and ECT was administered to another 5. Laboratory tests and serial EEG's were routinely employed. In a followup study, 14 improved patients received amitriptyline, 30-100 mg/day. Results indicated marked improvement in 16 (44%), moderate improvement in 11 (30%) and no improvement in 9 (26%). Weight gains were observed in 42 patients. Side effects included dry mouth, tremor, weak spells, dizziness and drowsiness, etc. In the followup study, 9 patients maintained satisfactory improvement on maintenance medication. Relapses were observed in 3 others after cessation of medication.

Dept. of Psy., U. of Tenn. Coll. of Med.
Nashville, Tenn.

2693 Jonas, P. Esucos (U.C.B. 3412). *Acta Neurologica et Psychiatrica Belgica*, 1961, **61**, 774-775.

Fifty cases of pathological thinness (without apparent organic cause), some treated previously with classic anabolizing agents, responded remarkable to 20-40 mg/day dixyrazine (UCB) 3412). Dixyrazine acted as if it were an anabolizing agent in all 50 cases, and after 3 months weight gains of 8-12 kg were attained.

No address]

2694 Kaivers, R. Esucos (U.C.B. 3412). Esucos (UCB 3412).] *Acta Neurologica et Psychiatrica Belgica*, 1961, **61**, 771-773.

Nineteen patients with functional disorders were treated with dixyrazine (UCB 3412), initially 25 mg t.i.d., then 10 mg t.i.d. with about $\frac{1}{4}$ of the patients taking 25 mg in the evening. Results were considered good in 14 out of the 19 cases but 5 cases showed intolerance: drowsiness even at low doses.

29, rue Maréchal Gérard
Antwerp, Belgium

2695 Cirilli, M., Bloch, F., & Uhry, P. *Traitement du delirium tremens par un nouveau neuroplegique*. [Treatment of delirium tremens with a new neuroplegic.] *Clinique*, 1961, **56**, 497.

Chlorprothixene was 82% successful in the treatment of 10 women and 50 men, most between 40 and 50 years of age, suffering from delirium tremens. Average duration of psychomotor agitation was 2.66 days and the average length of hospital stay 9 days. Initially 3 15 mg ampules were given i.m. every 4 hours for an optimal dose of 270 mg/day. Dosage was then dropped to 180 mg/day, i.e., 3 ampules every 6 hours. The only side effect noted was 1 case of tendency to collapse. The mortality rate was very low - 5%.

Hôpital de la Pitié
Paris, France

2696 Weil, Andre A. EEG observation in narcoleptic adults. *Diseases of the Nervous System*, 1962, **23**, 279-283.

EEG tracings of 21 narcoleptic subjects (15 narcoleptic attacks only, with concomitant cataleptic episodes and 3 with sleep paralysis), aged 17-54 years, were analyzed and records were obtained during free intervals and narcoleptic attacks. Characteristic findings in 76% included low voltage theta patterns corresponding to physiological states of drowsiness. Persistent EEG drowsiness patterns were noted in 7 subjects (33%) even during vigorous hyperventilation. Administration of deoxyephedrine or amphetamine i.v. produced waking records with good alpha spindling. EEG observations seem to implicate a reversible disturbance in the brain-stem reticular activating system.

Huron Road Hospital
Division of Neurology
Cleveland, Ohio

2697 Oybir, Fahrettin. Trifluoperazine in chronic, withdrawn schizophrenics. (A double-blind study). *Diseases of the Nervous System*, 1962, **14**, 348-350.

Trifluoperazine (2-20 mg b.i.d., p.o.) or placebo was administered on a double-blind basis to 29 chronic female schizophrenics (average duration of illness 24 years), average age 57 years, for 6 months. Results were rated by means of 75-item symptomatologic profiles. Eighteen were granted grounds privileges because of their obvious improvement. Patients showed increased sociability, communicativeness and activity, with emphasis on greater accessibility to group and occupational therapy. Hallucinations and interpersonal relations were particularly improved. Controllable side effects included restlessness, anorexia, parkinsonian reactions, excessive thirst, allergy, perspiration and dysphagia.

State Hospital for Mental Diseases
Howard, Rhode Island

2698 Haynes, Elmer, Blanchette, James, & Gericke, O.L. Experience with chlor-

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diazepoxide in Huntington's chorea. *Diseases of the Nervous System*, 1962, **23**, 326-328.

Chlordiazepoxide (30-150 mg/day) was administered to 9 patients with Huntington's chorea, aged 32-62 years, for several weeks. Anxiety symptoms decreased and mild euphoria was noticeable. Choreiform movements slowed to dystonic movements with improved coordination and equilibrium. Untoward effects consisted of dizziness, ataxia, drowsiness and leg weakness. Marked improvement was observed in 3 patients.

Patton State Hospital
Patton, Calif.

2699 O'Reilly, P.O., & Reich, Genevieve. Lysergic acid and the alcoholic. *Diseases of the Nervous System*, 1962, **23**, 331-334.

LSD (200 µg p.o.) was administered to 33 chronic alcoholics, aged 21-59 years, directly before a 2-hour psychotherapy session. Objective questionnaires were completed by patients 1 day after the LSD interview. A 7-88 week period of followup indicated that 7 abstained completely, 10 improved, 10 were unchanged and 6 provided no available reports. Therefore, 17 patients derived benefit from the LSD experience and 16 did not. Apparently, the LSD experience is useful in treating chronic alcoholism.

Psychiatric Department
Union Hospital
Moose Jaw, Saskatchewan
Canada

2700 Khosbin, A., & Guyotat, J. Essais clinique avec le Ro 4-1575. [Clinical trials with RO 4-1575.] *Annales Médico-Psychologiques*, 1962, **120**, 1, 310-311.

Forty-one depressed patients were treated with 150-250 amitriptyline p.o. Twenty-seven percent improved markedly, 29% slightly and 44% showed no results. The product was more efficacious in women than in men (33% compared to 12.5%). Tolerance was excellent but transitory paraparesis, aggravation of a hemiparesis and confusion. However the drug was less efficacious than imipramine.

[No address]

2701 Balatre, J., Berger, Cl., & Chirat, P. Etude clinique en milieu obstétrical d'un nouveau barbiturique: le 96 JD. [Obstetric study of a new barbiturate: JD 96.] *Lyon Médical*, 1962, **40**, 575-581.

5-Vinyl-5 (methylbutylmalonyl) urea - JD 96 - was employed clinically as a hypnotic in 50 patients. Half of the cases were women in good health before and after delivery, and the other half were women with disorders of pregnancies. It was not used as an analgesic in any case. Dosage was 1 or 2 100 mg tablets as a rule; rarely 100 mg suppositories were used. Results were excellent in 93% of cases and JD 96 was effective when phenothiazines, secobarbital or butobarbital were ineffective. The onset of drug effect took place at an average of 30 minutes with 1 tablet and in 20% of the cases sleep ensued in less than a quarter hour. Nightmares were very rare: 4%. No side effects were noted.

Service du Dr. Ed. Rochet
Hôpital de l'Hotel-Dieu
Lyon, France

2702 Robinson, J., McCabe, E., & Graves, Ch. Acepromazine. Un tranquillisant nouveau et très actif. [Acepromazine. A new extremely active tranquilizer.] *Clinique*, 1961, **56**, 593-594.

Acepromazine was given to 35 patients, including 17 schizophrenics. Average dosage was 100-200 mg i.v. on the 1st day continued as oral medication, 50 mg q.i.d. Seven cases showed excellent improvement, 10 good improvement, 9 fair results and 9 had poor reactions. No side effects were reported.

[No address]

2703 Ingvar, David, & Nilsson, Eric. Central nervous effects of neurolept-analgesia as induced by haloperidol and phenoperidine. *Acta Anaesthesiologica Scandinavica*, 1961, **5**, 85-88.

neuroleptanalgesia can be accepted as a fully adequate replacement for generalized anesthesia. EEG examinations of 7 laparotomy patients were made after premeditation with 5-10 mg haloperidol. When administration of phenoperidine [dosage unspecified] was begun and intubation carried out after succinylcholine, EEG recording was made continuously. Patients were instructed to answer simple questions by nodding or shaking their heads, etc. Phenoperidine produced general analgesia and severe respiratory depressions, but consciousness was reserved as demonstrated by typical waking alpha activity in all patients. As the mechanisms controlling wakefulness and respiration are closely associated, the splitting phenomenon revealed by these studies is pharmacologically unique and of neurophysiological interest.

Department of Neurology
University Hospital
Umeå, Sweden

2704 Libby, Harold E. The general practitioner and the alcoholic patient. *Journal of the Maine Medical Association*, 1962, **53**, 265-268.

Chlordiazepoxide (100 mg i.m. or p.o., then 10 mg every 3-4 hours diminished to 5-10 mg p.o. t.i.d. or q.i.d.) was administered to 75 alcoholics, aged 25-75 years, for 3 days to 7.5 months. Marked to moderate improvement occurred in 69 or 92%. The 11 with acute alcoholism were all controlled, and 47 of the 51 with uncomplicated chronic alcoholism showed marked to moderate gains. Side effects included drowsiness in 1, drowsiness and ataxia in 2, psychomotor agitation in 1 and senile psychosis with severe ataxia in 1. In all save 1 patient, side effects disappeared with dosage reduction.

Maine Chapter of the AAGP
Lafayette Hotel
Portland, Me.

2705 Kissen, Martin D. Management of acute withdrawal symptoms of alcoholism. *Missouri Medicine*, 1962, **59**, 965-968.

Eighty alcoholics received chlordiazepoxide

(100 mg i.v., i.m. or p.o. initially, then 10 mg p.o. q.i.d.) and 80 controls received placebo. Dose-response curves indicated that chlordiazepoxide was effective in alleviating the symptoms of acute alcoholism. In addition, 67 out-patients with postalcoholic tension state, aged 24-63 years, received chlordiazepoxide (10 mg b.i.d. to 25 mg q.i.d.) for 1 week-6 months. All except 5 reported relief from anxiety within 24 hours. No side effects were observed.

C. Dudley Saul Clinic
St. Luke's and Children's Medical Center
Philadelphia, Pa.

2706 Beck, D. Vegetative Untersuchungen, Therapie und Prognose der Erschöpfungsdepressionen. [Investigation of the autonomic system, therapy, and prognosis in exhaustion depressions.] *Schweizer Archiv für Neurologie Neurochirurgie und Psychiatrie*, 1962, **90**, 370-391.

Twenty patients (18 female, 2 male) suffering from manifold autonomic-somatic disturbances, were tested by means of the Schellong cold pressor-and rewarming tests. Pathological results were obtained in all 20 cases; 18 patients displaying hyperfunction of the nervous system with sympathetic hypertonia, the remaining 2 demonstrating hyperfunction without exhaustion symptoms. In addition to psychotherapy, bedrest and insulin administration (4-12 U) for 10-30 days in combination with a thymoleptic drug, e.g., imipramine (at doses 3×30 mg i.m., and 3×25 mg i.m. respectively or oral administration of 3×30 -90 mg and 10-50 mg respectively.) Cures were effected in 16 patients and improvement in 4. The exhaustion syndrome is generally due to chronic affective conflicts; it more frequently affects women and prognosis is good. A followup study of the patients revealed only 2 relapses.

Psychiatrische Universitätsklinik
Basel, Switzerland

2707 Lammers, H.J. Erfahrungen mit dem Psychopharmakon Truxal. [Experiences

with the psychiatric drug Truxal.] Therapie der Gegenwart, 1962, 101, 310-319.

Chlorprothixene (Truxal) tablets were administered at doses of 50-100 mg t.i.d. to 118 patients consisting of 60 depressives, 33 schizophrenics, 12 psychopaths, 6 older persons with paranoid psychoses or syndromes and 7 miscellaneous cases. Good results were obtained in 52 cases, moderate to doubtful results in 27 cases and failures in 31. Patients with endogenous depressions responded well, as did excitability, restlessness and anxiety states. Catatonics responded very poorly. Side effects were generally mild, consisting of tiredness, hyperhydrosis, nausea, dizziness, dry mouth and very slight extrapyramidal disturbances.

Psychiatrische Nervenklinik der Univ.
Giessen, Germany

2708 Niver, Edwin O. Carphenazine and the extrapyramidal regulation of kinesthetic function. Diseases of the Nervous System, 1962, 14, 340-348.

Carphenazine (75-900 mg/day) was administered to 20 chronic parkinsonian patients (duration of illness greater than 10 years), for 6 months and to 20 other patients for shorter periods of time. Results revealed an increase in affective response away from apathy, an improvement in quantity and quality of communication, an increased alertness and awareness of environment and behavioral improvements. Side effects constituted excessive sedation in patients who initially manifested excessive lethargy.

Mental Health Institute
Clarinda, Iowa

2709 Wiehler, H. Zur Behandlung der Depressionen mit Monoaminoxidasehemmern. [Treatment of depression with monoaminoxidase inhibitors.] Nervenarzt, 1962, 10, 462-466.

Fifty-two hospitalized patients were treated with isocarboxizide (Marplan). Forty-eight patients had depressions, 4 chronic schizophrenia. The dosage was 3-8 tablets

(10 mg each) per day for 4 weeks, in 9 cases 6-8 weeks, in 1 case for 14 weeks. The drug was very well tolerated. Depressions with agitation responded well; the severity of mood disturbances was lessened after 5-10 days, and relaxation of impulse inhibition could be achieved. In depression coupled with agitation and restlessness Marplan was administered in combination with a neuroleptic agent or sedative. Chlorprothixene and glutethimide [dosages unspecified] were effective for this purpose. Some minor side effects disappeared after reduction of the dosage. Three case histories are elucidated providing only general information.

Wahrendorffsche Krankenanstalte
Ilten-Köthenwald
Hannover, Germany

2710 Shawver, John R., Scarborough, James S., & Frank, Thomas V. Comparison of chlorpromazine with fluphenazine dihydrochloride in treatment of schizophrenics. Diseases of the Nervous System, 1962, 23, 392-395.

Initially, 28 acute schizophrenics received fluphenazine (2.5-20 mg/day p.o.) or chlorpromazine (200-400 mg/day p.o.) for 12 weeks. A 2nd phase involved administration of fluphenazine (1-5 mg/day p.o.) or chlorpromazine (100-400 mg/day p.o.) to 50 chronic schizophrenics for 4 months. Assessment procedures included joint evaluations by a psychiatrist and a psychologist, the MSRPP and combined ratings of a nurse and nursing assistant. The only significant side effects were extrapyramidal tract syndromes which were controlled with benztropine methanesulfonate and trihexyphenidyl. In addition, 35 patients received fluphenazine (2.5 mg/day p.o.) as maintenance therapy for 8 weeks. Both chlorpromazine and fluphenazine appear equally efficacious in controlling behavior in acute and chronic schizophrenics.

VA Hospital
Waco, Texas

2711 Oettinger, Leon, & Simonds, Robert. A new anticonvulsant (1-methyl-5-5-phe-

yl ethyl hydantoin) in treatment of epilepsy in children: a preliminary report. *Diseases of the Nervous System*, 1962, 23, 403-406.

Methetoin (40-90 mg/kg/day) was administered to 46 epileptic children, ages 6-13 years, for 5 days - 3 months. Of the 6, 18 experienced 75-100% control of seizures, while 14 showed 25-50% improvement. Toxicity was not a serious problem, and 2 cases of leukopenia were complicated by a flu epidemic. Methetoin is an effective anticonvulsant in patients who have been resistant to other anticonvulsants.

EEG Department
St. Luke Hospital
Pasadena, Calif.

2712 D'Amato, Gabriel. Chlordiazepoxide in the management of school phobia. *Diseases of the Nervous System*, 1962, 23, 292-295.

Chlordiazepoxide (10-30 mg/day with 10 mg at bedtime) was administered to 9 children, aged 8-11 years, with school phobia who were undergoing family psychotherapy. Only 1 child failed to maintain regular school attendance after the 2nd week of treatment and the remaining 8 were vastly improved. Transient drowsiness in 1 child constituted the only side effect. Chlordiazepoxide was extremely effective in enabling children to relinquish their tenacious hold on the mother and return to school.

Eugene Talmadge Memorial Hospital
Augusta, Ga.

2713 Chesrow, Eugene, J., Musci, Joseph P., Kaplitz, Sherman E., Sabatine, Raoul, & Levine, Jacob M. Use of ethyltryptamine acetate in parkinsonism and senility with depressive states. *Geriatrics*, 1962, 17, 137-141.

Ethyltryptamine (10 mg b.i.d. increased to 5 mg t.i.d. for the last 2 weeks) was administered to 18 patients (10 Parkinson's syndrome and 8 paralysis agitans), aged 38-74 years, and 27 patients with

reactive depression, aged 43-66 years, for 5-7 weeks. Control groups received placebos, and all groups received extensive laboratory testing. Patients chosen at random were evaluated by means of the SRA Non-Verbal and the Thurston Temperament Tests. Of the 17 receiving psychometric evaluation, results were 7 excellent, 6 good, 4 questionable and 0 negative. Of 9 with parkinsonism, 7 showed poor responses and 2 did not change. About 1/3 experienced drowsiness and minor tremulousness during the first 10 days of treatment. Symptoms disappeared upon continuation of therapy. An additional 30-day study was performed in which 9 patients with severe rigidity and tremor received ethyltryptamine (15 mg t.i.d.). Therapy was discontinued in 2 due to marked increase in tremors and rigidity, 2 manifested no change, 1 became more cheerful and the remaining 5 continued to regimen despite deterioration of their condition.

Department of Medicine
Oak Forest Hospital
Oak Forest, Ill.

2714 De la Fuente, Muniz, Ramón, & Martinez Cid, Enrique. El G33040 (Insidon) en el tratamiento de las disfunciones viscerales psicogenicas. [G 33040 (Insidon) in the treatment of psychogenic visceral disfunctions.] *Prensa Médica Mexicana*, 1962, 5, 208-210.

Thirty-six patients, aged 23-62 years, were treated with 50-200 mg piperazinoiminostilbene (Insidon) p.o., in 3 divided doses. Duration of treatment was 3-18 weeks. Conditions included gastritis, enteritis, circulatory and respiratory disorders, tension headache, etc. Aside from its anxiolytic effect, the drug has a regulatory effect on visceral activity. Twenty-five out of the 36 (64.1%) patients improved. Five showed slight dry mouth, and 6 restlessness and increased anxiety in the first 3 days. Five showed slight drowsiness. In 5 cases where the drug was intentionally withdrawn, symptoms reappeared; later after meprobamate and chlordiazepoxide had been tried, piperazinoiminostilbene was reinstituted and rapidly controlled symp-

Clinical studies
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toms.

Servicio de Psiquiatría
Hospital Español
Mexico City D.F., Mexico

2715 Hamilton, L. Dean, & Bennett, Jesse L. Acetophenazine for hyperactive geriatric patients. *Geriatrics*, 1962, 17, 596-601.

Acetophenazine (20-60 mg/day p.o.) or placebo was administered on a double-blind basis to 27 hyperactive, psychotic men (19 organic brain disease with psychosis, 7 schizophrenia and 1 depression), mean age 71 years, for 3-8 weeks. Patients were rated by ward personnel on a scale based upon 13 target symptoms. Results showed that 13 (68%) showed a significant decrease in hyperactivity, 6 (31%) were mildly improved and 7 (37%) were moderately improved. Three were unchanged and 3 became worse. Controls showed 8 (25%) with significant improvement and 6 (75%) who failed to change appreciably. Maximal improvement began in 3-4 weeks. Giddiness and lethargy constituted the principle side effects in 37 and 26% respectively.

VA Hospital and University
Utah College of Medicine
Salt Lake City, Utah

2716 Neilson, Duncan R., & Neilson, Ronald P. Clinical evaluation of iproniazid in obstetrics. *Western Journal of Surgery, Obstetrics and Gynecology*, 1962, 70, 191-198.

Iproniazid (25 mg b.i.d. for 1 week, then 25 mg/day) was administered to 80 pregnant women (6 chronic recurrent depression, 5 postpartum psychosis, 51 constitutional fatigue syndromes with depression and 18 mixed emotional and behavioral disorders). Maintenance therapy varied from 12.5-37.5 mg/day for 5-90 days. All 6 with recurrent depression responded with gratifying results, as did those with postpartum psychosis. About 90-95% of those with constitutional fatigue syndrome manifested genuine improvement

The miscellaneous group showed 80% improvement overall. Side effects include hepatotoxicity, transitory jaundice, insomnia, hyperactivity and muscular twitching.

[No address]

2717 Batten, Charles T. Long-release barbiturate medication for relief of tension. *Medical Times*, 1962, 90, 1213-1218.

A sustained release capsule of pentobarbital (100-200 mg/day p.o.) was administered to 24 psychiatric patients, aged 25-68 years, for 4-5 months. Overall results were optimal in the geriatric group of 9 elderly women with CBS. Clinic patients (3 emotionally unstable) were erratic in taking medication and unreliable in reporting results. The geriatric patients were far more manageable, with fewer complaints and less apprehension after phenobarbital administration. Of the private patients, 3 failed to improve, 1 showed relief of tension with persistent depression and 1 exhibited very gratifying overall improvement. Occasional drowsiness constituted the only side effect. Phenobarbital is apparently well suited for alleviation of transient tension.

Department of Psychiatry
Loma Linda University
Los Angeles Campus
Los Angeles, Calif.

2718 Broussolle, P. A propos de quatre années d'expérience de la prochlorpémazine en psychiatrie. [On four years of experience with prochlorpemazine in psychiatry.] In: Baruk, Henri, & Launay, Jacques [Eds.] *Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.* Paris: Presses Universitaires de France, 1962. Pp. 79-81.

In 4 years of clinical experimentation some 500 patients have been treated with prochlorpemazine; starting doses were 50-150 mg/day, increased to 600 mg/day p.o. Both the oral and i.m. routes were used,

the latter in periods of crisis. The drug is particularly effective in states of agitation, and indicated in auditory hallucinations, states of delirium and schizophrenic dissociation. It is particularly useful in chronic schizophrenia including paranoia, aggressiveness and agitation. Side effects, e.g., extrapyramidal syndrome, are similar to those seen with chlorpromazine.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2719 Baruk, H., Launay, J., Tardy, C., Boige, P., & Bricout, J. Expérience clinique de la prochlorpémazine. [Clinical experience with prochlorpémazine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 82-88.

Sixty-three patients, including 16 cases of atypical schizophrenic depression, 11 catatonias and 11 cases of hebephrenia, were treated with progressively increasing doses of prochlorpémazine (10 mg b.i.d. reaching 20-80 mg/day). Duration of treatment was 1-10 months with an average of 4-5 months. Forty-seven percent improved, 42% did not and 11% were aggravated. Only 1 case of tremor occurred wherein cessation of treatment was necessitated; however this patient had previously suffered from chorea. Also a case of oculogyric crisis was noted. Extrapyramidal signs occurred in a total of 9 out of 81. Psychomotor improvement occurred and some slight tachycardia, nausea and psychomotor excitation were observed.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2720 Launay, J., & Conté, C. Etude expérimentale et essais thérapeutiques du 1522 C.B. ou acépromazine. [Experimental study and therapeutic trials of CB 1522 or acetopromazine.] In: Baruk, Henri,

& Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. 89-98.

Experiments with progressively increasing doses of acepromazine are reviewed using pigeons, guinea pigs, mice and monkeys. Secondly, clinical trials with 30 patients (3 melancholic depression, 5 atypical schizophrenic depression and 22 cases of schizophrenia) are detailed. All dosages of acepromazine were 10-100 mg/day in 2 doses and treatment lasted 3-3½ months. The 3 cases of melancholia were worsened after 15 days to 3 weeks of treatment, necessitating the cessation of therapy. One case of atypical schizophrenic depression improved remarkably, while 3 did not improve and the 5th was worsened (appearance of excitation). Of the 22 schizophrenics 2 improved, 5 became worse with manifestations of aggression and impulsiveness. 1 became more apathetic and the remaining 15 did not change appreciably. Slight arterial hypotension and tachycardia were noted along with extrapyramidal signs. In relation to the blood picture, there was no significant modification though a slight increase in sedimentation rate and some slight leucocytosis. The drug is indicated for neurosis and anxiety, not major psychiatric conditions.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2721 Gurtler, J. & Goralsky, G. Essai thérapeutique du tartrate d'alimémazine (Théralène) portant sur 415 malades psychiatriques sur une période d'environ trois ans. [therapeutic trial of alimemazine tartrate (Theralene) in 415 psychiatric patients over a period of about three years.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 113-121.

Clinical studies
Abstracts 2722-2724

Four-hundred-and-fifteen cases treated with alimemazine included 113 cases of melancholia, 71 neurosis, 67 schizophrenia and 68 cases of delirium. All patients were women. Parenteral administration was employed as well as the more usual use of tablets, syrup and suppositories. Dosage was progressively raised to 450 mg/day or 150 mg t.i.d. whereafter dosage was progressively diminished to 120-180 mg/day. Results (when 28 cases of senile dementia, oligophrenia and 12 cases of epilepsy were omitted leaving 357 cases) were 25.9% cured, 34.7% failures.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2722 Gurtler, J. & Goralsky, G. Tracés électro-encéphalographiques au cours de traitements par le tartrate d'alimémazine. [Electroencephalographic tracings in the course of treatment with alimemazine tartrate.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 124-131.

Anomalies in EEG tracings have frequently been observed after 10-15 days of alimemazine treatment at 30-60 mg/day. Modifications consist of spontaneous dysrhythmic elements (often appearing as precursors to epileptogenic manifestations), typical spikes and sometimes a slowing in a rhythm. However towards the end of the treatment the tracing is often improved or even normal. Of 28 patients, 17 presented abnormal EEG's before treatment, and dysrhythmias remained in these cases after clinical cure. Alimemazine acts as a catalyst for the accentuation of existing EEG abnormalities, but deviations lessened as treatment progressed and the drug does not appear to be a true epilepsy-inducing agent.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2723 Verdeau-Pailles, Jacqueline. Tolérance locale et efficacité de la promazine. Comparaison avec la chlorpromazine. [Local tolerance and efficacy of promazine. Comparison with chlorpromazine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 132-135.

Twelve patients received 3 i.m. injections of promazine as a substitute for oral chlorpromazine therapy. One group received 75 mg/day promazine for 15 days, while another received 150 mg/day for 8 days. Efficacy at the 150 mg level of promazine was equivalent to that of 100 mg chlorpromazine p.o. Local and general tolerance for promazine was excellent. Slight tachycardia was frequently observed in patients on 150 mg/kg and 5 cases of rise in body temperature were noted.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2724 Fouks, Lainé, Pagot, & Ferrant. Note sur le G 22 355 (imipramine). [Note on G 22 355 (imipramine).] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 149-152.

Imipramine (i.m.) [dosage unspecified] produced appreciably good results in about 50% of 32 depression cases which were resistant to other therapies. Four patients were markedly aggravated by drug induced excitation and 1 of these suffered confusion. Marked improvement was noted in 9 cases of melancholia out of 21 and slight improvement in 9 others. Negative results were obtained in 10 cases of neurotic depression. Slight extrapyramidal reactions usually developed by the 2nd week.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2725 Baruk, H., Launay, J., Tardy, G., Boige, P., & Bricout, J. Premiers résultats d'essais thérapeutiques de l'imipramine ou G 22 355. [Initial clinical results with imipramine or G 22 355.] In Baruk, H., & Launay, J. [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 153-156.

Increasing doses (25 mg ampules) of imipramine were used in 32 cases of depression reaching 300-350 mg/day. Oral dosage was also used, good results being obtained with relatively low doses, i.e., 6 tablets or 100-150 mg/day. Of 16 cases of melancholic depression, 7 improved markedly, 4 showed no effect and 5 were aggravated with an increase in anxiety and agitation. Of 10 cases of catathymic depression, 7 showed major improvement and 3 were worsened. The 2 cases of senile melancholia treated improved markedly. The 3 cases of depression with psychasthenia and obsessional components also improved notably with the rapid reduction of obsessional ideas. One catatonic woman showed clear improvement. In 10 out of the 32 cases that were worsened, anxiety and agitation were the chief downward effects, and in 5 out of the 8 these signs were accompanied by extrapyramidal reaction.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2726 Lambert, P.-A. Sur quelques remarques concernant l'utilisation de l'imipramine (G 22 355 ou Tofranil N.D.) en pratique psychiatrique hospitalière et extra-hospitalière. Association avec les neuroleptiques et l'iproniazide. [Some remarks concerning the use of imipramine (G 22 355 or Tofranil N.D.) in hospital and extra-hospital psychiatric practice. Combination with neuroleptics and iproniazide.] In: Baruk, H., & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris:

Presses Universitaires de France, 1962. Pp. 157-15

Indications for imipramine are discussed: the melancholic type of depressive reaction, manic depressive psychosis, presenile depression, etc. These remarks are accompanied by 6 case reports. The rapidity of imipramine's action, the common attainment of approximately 50% success and side effects such as parkinsonism are recorded.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2727 Baruk, H., Launay, J., Cournut, J., Vallée, A., & Tardy, C. Le problème des indications thérapeutiques, des doses et des incidents de traitement par l'imipramine après une expérience de 18 mois. [The problem of therapeutic indications, dosage and side-effects with imipramine after an 18-month experience.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 164-172.

Nineteen cases of anxiety, 14 asthenic syndrome, 10 erythismus, 9 cenesthesia (including depersonalization), 12 neurotics with ideas of ruin, etc. with or without delirium, 7 obsessional reaction and 8 treated with imipramine. Oral dosage was begun with 25 mg once or twice a day, raised to an individual optimum for each case, usually 100-150 mg/day, modified in cases of marked improvement to 50-75 mg/day. Cases intense intolerable dry mouth necessitated interruption of treatment. Imipramine was often combined with levomepromazine, alimemazine, meprobamate and other substances. Other imipramine side effects noted were drop in arterial tension, slight leukocytosis, extrapyramidal reaction including hypotonia of the arms, psychomotor tension and insomnia, etc. Results were considered successful in 42 out of the 65 cases. Brief note was also made of successful therapy with imipramine and chlordiazeposide in combina-

tion.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2728 Coirault, R. Une orientation thérapeutique nouvelle en neuropsychiatrie et en pathologie générale. L'ester-diméthyl-amino-éthyl-ique de l'acide para-chlorophénoxy-acétique (A.N.P. 235). Psychocortico-tonique régulateur des fonctions hypothalamo-hypophysaires et neuro-régulateur central. Action sur les troubles de la conscience. Étude clinique biologique, électro-encéphalographique et psychométrique. [New therapeutic orientation in neuropsychiatry and general pathology. The dimethylaminoethyl ester of parachlorophenoxy acetic acid (ANP 235). Psychocorticotonic, regulator of hypothalamohypophysis functions and central neuro-regulator. Action on mental disorders. Clinical, biological, electroencephalographic and psychometric study.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 173-183.

One-hundred- and-seventy-seven cases (76 cranial trauma, 29 endocrine disturbance with hypothalamo-hypophyseal origin and 72 psychiatric cases - 35 cases of simple neurosis, 22 depression, etc.) were treated with centrophenoxine. Conventional oral dosage was 400-800 mg/day. A dose as high as 4 g/day was found nontoxic. Benton's test and the Rorschach were used in evaluation along with EEG reports. Its effects on anxiety-insomnia-fatigue were considered excellent and centrophenoxine augmented lucidity and intellectualization. It had a regulatory effect on the hypothalamo-hypophyseal axis, improving the general metabolism. It also had a possible effect on the reticular system, providing improvement in hypertonic states. The agent is considered as a psychocorticotonic and central regulator.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2729 Launay, J., & Michelin, J. Action de l'A.N.P. 235 (Lucidril) sur les états confusionnels aigus et subaigus de l'éthylisme chronique. [Action of ANP 235 (Lucidril) on acute and subacute confusional states of chronic alcoholism.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 157-163.

Ten cases of delirium tremens were treated with centrophenoxine (usually 500 mg i.v.) for 7-8 days followed by 250 i.m. for a week or longer. This group was compared to a group of 13 who did not receive centrophenoxine. Chlorpromazine, other tranquilizers and vitamins were also used. One patient died of causes unrelated to drug administration and the remaining 9 improved notably at about 48 hours, whereas the group which was not treated with centrophenoxine showed improvement at 4-5 days. Additionally 1 man in a state of confusion, being treated with disulfiram was successfully controlled with centrophenoxine.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2730 Fouks, Lainé, Mathis, Pagot, Ferrant, Delavalade, & Riou. Étude sur l'effet du 2038 M.D. [Study of the effect of MD 2028.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 194-223.

MD 2028 (fluomethoxyphenylpiperazine butyrophenone) has given best results in states of acute agitation. MD 2028 is the best available drug for psychiatric emergencies. Several routes of administration are used, the i.m. route being preferred. Sixty-nine cases were treated, both psychiatric and alcoholic states. Intravenously the agent is used in 5 mg injections, up to 60 mg/day. Intramuscularly, 10-20 mg injections are

sed, not surpassing 80 mg/day. Using the oral route doses of 40-120 mg/day are optimal. Reserpine, levomEPROMAZINE and other drugs were also used in combination with MD 2028. Hypnotic effects were very rapid and MD 2028 appeared to potentiate sedatives. By the oral route, even in small doses the drug frequently causes digestive upset, and sometimes lypothymia. Additionally the drug activates patients with hebephrenic schizophrenia and similar conditions.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2731 Pariente, M. Le traitement d'attaques des états psychopathiques aigus par le MD 2028 M.D. [Treatment of acute psychopathic states with MD 2028.] In: Baruk, Henri, Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. 224-228.

MD 2028 is available in 10 mg ampules and 20 mg tablets. The i.v. route has been abandoned because of side effects (e.g., nausea), and the i.m. route is recommended. A dose of 10-20 mg i.m. at one time is that most often used for the control of crises. Agitation and excitation are immediately relieved due to its sedative effect. Local tolerance is excellent. The case load treated was 31 acute or subacute cases of alcoholism, 17 acute schizophrenia, 13 agitation, 10 manics and depressives, 9 acute states with delirium, 7 senile agitation, epilepsy and 7 miscellaneous cases. Side effects were minor and included nausea, vomiting, general malaise with pallor and transitory tachycardia, lacrimation, headaches, constipation with retention of urine, etc.

Établissement Psychothérapique de Fleury-les Aubrais
Charenton-le-Pont, France

2732 Fouks, Lainé, Pagot, Mathis, Ferrant, Delavalade, & Riou. Rapport sur l'essai clinique de la phénelzine. [Report on a clinical trial with phenelzine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. P. 234-242.

Phenelzine is an excellent thymoleptic with rapid and efficient action. Twenty-eight cases of neurotic depression, 28 manic-depressive psychotics, 25 chronic and involutional melancholia, 17 simple depression and 3 miscellaneous cases of mental illness were treated with 90 mg/day phenelzine given on waking, in the middle of the morning and at noon, for the first 10 days. In the next 10-15 days 60 mg was given each day. Fifty cases were studied encephalographically. Twenty of these cases showed no constant modification, while 30 did. Basic alpha rhythm was regularized and improved with increase in amplitude in 14 cases, but in 11 cases there was a drop in voltage with alpha waves more discontinuous and irregular. In a few cases alterations in the beta band were also noted. The drug not only alleviated depression but also favorably affected apathy. The only notable side effect was a frequency of hypotension.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2733 Baruk, H., & Richardeau. Essais de la phénelzine en thérapeutique clinique. [Trial of phenelzine in clinical therapeutics.] In: Baruk, Henri, & Launay [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 243-252.

Twenty-four women with mixed chronic

Clinical studies
Abstracts 2734-2736

psychiatric conditions were treated orally with 15 mg phenelzine b.i.d. or t.i.d. Results were recorded as: 11 improvements, 4 no effect, 3 aggravations and 6 blood pressure or vasomotor disturbance. Results were considered particularly good in cases of obsessional states. Cardiovascular disturbances were frequent, i.e., a moderate bradychardia (60-70) repolarization with flattening of the T wave in a 3rd of the cases, and progressive severe hypotension with postural hypotension in all cases after the 25th day of treatment. In the 6 cases noted above this hypotension necessitated interruption of chemotherapy, i.e., difficulty in visual accommodation, weakness in the legs, fainting, etc. This hypotension is resistant to common analeptics and epinephrine. Also it was not modified by perlingual epinephrine. When neuroleptics were used with phenelzine in some cases while they did not potentiate the phenelzine hypotension, but they did favorably modify bradycardia due to phenelzine.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2734 Fouks, Ferrant, Lainé, Mathis, & Pagot. Rapport sur l'essai clinique de l'iproniazide en psychiatrie. [Report on a clinical trial of iproniazid in psychiatry.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 253-255.

Treatment of 88 patients was begun with 200 mg/day iproniazid rapidly reduced to 100 mg/day and even 25 mg/day. Iproniazid was in general combined with reserpine or chlorpromazine in the treatment of schizophrenics. The caseload included a proportion of depressives and many included a proportion of depressives and many elderly patients, some arteriopathic. Iproniazid is an energizer and a euphoriant, and appears indicated in various cases of depression. Some patients, including elderly ones, showed improved behavior, activity and intellectual ability. The most clear

and constant pharmacological effects are cardiovascular: 42 cases of marked hypotension have been observed. Some patients show abrupt changes in blood pressure which appear dangerous and additionally ECG alterations are frequent.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2735 Ullery, John C., & Bair, Janes R. Maternal-fetal effects of propiomazine-meperidine analgesia. American Journal of Obstetrics and Gynecology, 1962, 84, 1051-1056.

Initially, 100 women in labor received 50 mg pethidine (meperidine) and 20 mg propiomazine i.v. Then, 165 patients received the propiomazine-pethidine combination i.v. or 50 mg of pethidine alone in a double-blind study to determine maternal and newborn effects. In the 1st study, 91% had good to excellent analgesia, 96% comparable sedation. With both pethidine and the combination, 91% of infants had excellent Apgar ratings. In the 2nd study, the combination of pethidine - propiomazine gave significantly greater analgesia, sedation, and relief of anxiety and apprehension than did pethidine alone. No hypotension occurred, but transient hypertension developed in 3.25%. Of hypertensive patients, 30% showed a transient rise in pressure following medication. Only 1 dose was adequate in 71.5%. The amnesic effect was not pronounced.

Department of Obstetrics and Gynecology
College of Medicine
Ohio State University
Columbus, Ohio

2736 Faiaz, Esmail, Sreim, Eugene, & Calloway, William. Promazine and promethazine alone and in combination with obstetrics. Western Journal of Surgery, Obstetrics and Gynecology, 1962, 70, 92-95.

Promethazine plus promazine (50 and 50 or 25 and 25 mg) was administered to 79, 232 and 70 obstetric patients, respec-

tively (mean ages 26, 23 and 26 years), in conjunction with pethidine (50 mg) to determine efficacy of analgesia, amnesia, antiemesis and sedation. Blood pressure was monitored during all 3 stages of labor. Therapeutic effects were excellent or good with promethazine in respect to analgesia (61%), amnesia (27%), antiemesis (99%) and sedation (66%). With promazine, excellent to good results were as follows: 80% analgesia, 63% amnesia, 96% antiemesis and 75% sedation. Combined drug effects included: 79% analgesia, 59% amnesia, 98% antiemesis and 86% sedation. The combination was not superior in analgesic or amnesic effect to promazine alone, but both promazine and the combination were superior to promethazine alone. The combination was more effective in inducing sedation. Blood pressure increased with all 3 groups, but promethazine produced the greatest increase in systolic pressure. Antiemesis was excellent in all groups. More than 90% of the infants were adjudged in excellent condition. Duration of labor did not differ significantly and no variation was observed in requirements for anesthetics.

Department of Obstetrics and Gynecology
Lincoln Hospital
Lincoln, Neb.

2737 Baruk, H., & Richardeau. Etude sur l'essai thérapeutique du méthaminodiazépoxide. [Study of a therapeutic trial with chlordiazepoxide (methaminodiazepoxide).] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 260-264.

Fourteen hospitalized and 7 ambulatory patients were treated with oral chlordiazepoxide, usually 20-75 mg/day in 2 or 3 divided doses. Most of the patients were 40-60 years of age. Anxiety was a common symptom. The therapeutic dose approximated 30 mg/day and if this was ineffective then treatment was abandoned. Of 11 cases of anxiety - melancholia, 4 improved markedly, 3 partially, 1 very

lightly and 3 did not improve. One case of schizophrenia with anxiety improved slightly and another partially. Of 4 cases of obsession, 2 improved markedly and 1 partially; the other case was worsened. One patient with simple depression was cured. The last case, depersonalization, was very slightly improved.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2738 Fouks, Lainé, Périvier, Boucher, Mathis, Ferrant, & Riou. Rapport sur l'essai clinique du S. 186 (3,3-pentaméthylène-4-hydroxybutyrate de sodium). [Report on a clinical trial with S 186 (3,3-pentamethylene-4-hydroxybutyrate sodium).] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 265-274.

For periods of 6 months, S 186 was used in depression, particularly senile depression. Results on 51 patients are presented; usual dosage was 25-150 mg/day. This central analeptic caused improvement in general tonus as well as cardiovascular tonus, improved attention and mentation. It is particularly recommended in cases of apathy.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2739 Coirault, R., Jarret, R., Girard, V., & Desclos, S. Intéret de la fixation thyroïdienne du radio-iode I 131 dans les troubles psychopathologiques. [The importance of thyroid fixation of radio-iodine, I¹³¹ in psychopathologic disorders.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 324-332.

One-hundred-and-fifty psychiatric patients were studied in regard to iodine fixation ($25 \mu\text{c I } 131$). Most patients suffered the triad anxiety-insomnia-fatigue. Iodine uptake was abnormal in 65% of the males and 36% of the females at 24 hours. The curve for psychiatric patients paralleled that for normal subjects but was higher, i.e., 50% fixation at the 6th hour reaching 60% fixation at the 24th hour.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2740 Coirault, R., Jarret, R., Girard V., Desclos de La Fouchais, S., Péchery, C. Cortico-surrénale et psychopathologie. Les dosages des corticoides et la thérapeutique cortico-surrénale. [The adrenal cortex and psychopathology. Assay of corticoids and cortico-adrenal therapy.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 333-341.

Psychoendocrinological factors were studied in 150 psychiatric patients and 600 general patients as controls, i.e., 11 oxy-steroids and 17-ketohydroxysteroids. Variations in the urinary excretion of steroids was also studied following ECT, ACTH injection and insulin shock therapy. The excretion of 11-oxycorticosteroids by mental patients was less than that by general patients, and the excretion of 17-ketosteroids was much reduced in psychiatric cases. However in some cases of paranoid schizophrenia the excretion of 17-ketosteroids was elevated. Electrolyte balance, and the therapeutic use of ACTH, cortisone and triamcinolone was outlined.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2741 Coirault, R., Masbernard, A., Desclos de la Fouchais, S., & Mazingant, F. L'acide uridine-5-triphosphorique-

(U.T.P.). Thérapeutique majeure des atrophies musculaires (dystrophies musculaires, atrophies neurogènes). Influence sur les états de fatigue. Action neurostimulante. Contrôles biologiques et électrologiques. [Uridine-5-triphosphoric acid (UTP). Major therapy of muscular atrophies (muscular dystrophy, neurogenic atrophies). The influence on fatigue states. Neurostimulating action. Biological and electrologic control.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. -- Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 342-348.

Nine cases of progressive muscular dystrophy, 1 myasthenia, 30 neurogenic muscular atrophy, 30 fatigue and 10 anxiety-insomnia-fatigue were treated with uridine-5-triphosphoric acid (UTP; 10-20 mg/day p.o.). The agent was ameliorative in muscular dystrophy, myasthenia, neurogenic muscular atrophy, and particularly efficacious in fatigue. No side effects were noted.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

2742 Büssow, Hans. Vergleich der Wirkung zweier Glutarimide bei neuroleptischen Zuständen. [Comparison of the effect of 2 glutarimides in neuroleptic conditions.] *Medicina Experimentalis*, 1962, 6, 113-117.

A comparative investigation was carried out on 29 patients with acute or subacute endogenous psychoses, using Ba 12 408 (N-methyl- α -phenyl- α -ethylglutarimide) and glutethimide. All patients were pretreated with neuroleptic agents for 6-8 days; thereafter, either Ba 12 408 (100-200 mg t.i.d. or q.i.d.) or glutethimide (125-250 mg t.i.d. or q.i.d.) were administered in addition. Ba 12 408, which has no or only very slight anticholinergic effect, has no influence on mood changes in psychoses pretreated with neuroleptic agents; whereas glutethimide which has anticholinergic action is convincingly effective in bringing

about mood changes. This suggests that influences acting upon the centers responsible for central autonomic control play a significant part in the therapeutically desirable modification of the psychotic condition. An effect of glutethimide on central parasympathetic substrates in man must be considered, distinguished from the peripheral parasympatholytic action commonly seen experimentally in animals.

Psychiatrische Abteilung des Allgemeinen
Krankenhauses Ochsenzoll
Hamburg-Langenhorn, Germany

2743 Stelter, E. Über die Wirkung von Taractan bei vorwiegend chronischen Anstaltspatienten. [The effect of Taractan in predominantly chronic institutionalized patients.] *Therapeutische Umschau*, 1962, 19, 249-252.

Forty-five institutionalized chronically ill patients were treated with 30-50 mg chlorprothixene t.i.d. All patients had been treated with other psychoactive drugs and with ECT for a prolonged period. The most favorable effect was seen in agitated manic-depressive patients, and in patients with hypochondric mood disturbances. Improvement was occasionally also achieved in chronic schizophrenics; mood, agitation, motor unrest, and general condition of the patients could be favorably influenced. The drug was well tolerated; only in larger dosage (up to 450 mg/day) was lowering of blood pressure observed. It is doubtful whether some cases of slight anemia were actually caused by chlorprothixene.

Kantonale Heilanstalt
St. Pirminsberg, Switzerland

2744 Schmittkamp, H.J. Über die Wirkung eines Thioxanthenderivates ("Taractan") bei Hirntraumatisierten. [The effect of a thioxane derivative (Taractan) in patients with brain injury.] *Therapeutische Umschau*, 1962, 19, 159-161.

Thirty-two patients with concussion of the brain (8 of these in connection with skull fracture) were treated with chlorprothixene

(Taractan) for several weeks. The daily oral dosage varied from 30-120 mg during the 1st 1 or 2 weeks, and from 15-90 mg during the following 1 or 2 weeks. Headache and nausea improved so much that no additional therapy was necessary. Three patients developed minor allergic reactions and 3 patients did not respond.

Kantonsspital
Frauenfeld, Switzerland

2745 Meier, Paul J. Erfahrungen mit Neurocil in der Chirurgie. [Experiences with Neurocil in surgery.] *Therapie der Gegenwart*, 1962, 101, 322-325.

Levomepromazine (Neurocil; 0.025 gm i.m. or i.v.), a phenothiazine derivative, was used for the preparation of 163 patients for, mostly major, abdominal operations. It was administered once or twice, usually in combination with other drugs such as phenobarbital. The excellent sedating effect allowed considerable reduction in the use of analgesics. Nausea and vomiting were almost completely absent and blood pressure changes were minimal. A few older, arteriosclerotic patients responded with marked increase in blood pressure. Good results were also seen when levomepromazine was used in severely painful conditions.

Chirurgische Abteilung des St. Josef-
Krankenhauses
Troisdorf/Siegbach, Germany

2746 Gross, H., & Kaltenbäck, Elfriede. Sordinol R, ein neues Neuroleptikum der Thioxanthengerie. [Sordinol, a new neurolepticum of the thioxanthene group.] *Wiener Klinische Wochenschrift*, 1962, 74, 549-554.

A chlorprothixene analogue (Sordinol) has been shown to produce in animals effects similar to those of chlorprothixene. It was used in the treatment of 139 hospitalized patients, 131 of them schizophrenics. Single oral or i.m. dosages varied from 5-75 mg, and daily dosages from 10-225 mg (average 30 mg). The drug was generally tolerated; minor local in-

filtrations occurred from time to time, sleepiness and tiredness frequently. Extrapyramidal side effects mixed with anticholinergic and/or antiadrenalgic effects, hypotonia and tachycardia were also seen rather often. Side effects were tolerable in most patients or could be controlled with additional medication. Blood counts, blood chemistry and urinalyses showed no pathological findings. The drug should be administered to hospitalized patients only. Fifty patients showed minor improvement; 35 others showed no improvement. The remaining 54 patients were released as cured. Among these were many who have not responded to other neuroleptic agents. The effect of Sordinol is considered superior to that of chlorperphenazine.

Heilabteilung für Männer der Heil- und
Pflegeanstalt der Stadt Wien "Am
Steinhof"
Vienna, Austria

2747 Gross, H., & Langner, E. Prophylaxe und Behandlung des medikamentös bedingten Parkinson-Syndroms mit Procyclidin-Hydrochlorid (Kemadrin^R). [Prophylaxis and treatment of drug-induced Parkinson-syndrom with procyclidine-hydrochloride (Kemadrine^R).] Wiener Klinische Wochenschrift, 1962, 74, 569-570.

Procyclidine (Kemadrin) was used for the treatment of drug-induced postencephalitic parkinsonism. In comparison with atropine, its central effect is more pronounced, its peripheral effect 25 times weaker. Sixty-eight hospitalized and ambulatory patients were treated (5-15 mg t.i.d. p.o. and/or i.m.). A double-blind study was carried out with a group of 42 of these schizophrenic patients who had been treated previously with various neuroleptic agents. No effect was seen in 13 out of 14 patients who received the placebo. Good results were obtained in 19 out of 28 patients who had received procyclidine. The symptoms of the abulic-akinetic syndrome could be influenced very effectively in 95% of the patients. After disappearance or improvement of the akinetic syndrome, akathisia and akinesia could frequently be observed. These symptoms could be sufficiently improved with procyclidine in 43% (30-45 mg

per day). Tremor could be influenced in 33.3% of all cases. Paroxysmal dyskinesia could be controlled within 10 minutes with 5 mg procyclidine i.v. With simultaneous administration of 5 mg i.m., recurrent could be avoided. It is not suited for the treatment of parkinsonism caused by a neuroleptic agent with atropinelike side effects. The side effects were various but not unmanageable. Dehydration of mucous membranes was noted in 51.6% of the caseload.

II. Hals-, Nasen- und Ohrenklinik der
Universität Wien
Vienna, Austria

2748 Iranyi, Klara. LSD-Untersuchungen an ES-behandelten Schizophrenen. [LSD treatment in schizophrenic patients pretreated with electro-shock.] Schweizer Archiv für Neurologie, Neurochirurgie und Psychiatrie, 1962, 89, 413-425.

Eight female schizophrenic patients (16-48 years old) were treated with LSD (50-125 μ p.o.) before and after ECT; effects and reactions were compared. When LSD was administered before ECT, the following autonomic symptoms were observed: changes in blood pressure and pulse frequency, tremor, increased reflexes, positive Romberg, sweating and nausea. The psycho-organic syndrome developing after ECT was accompanied by various autonomic symptoms, such as: increased appetite, thirst, increased perspiration, muscle hypotonia and increased saliva secretion. There was less autonomic reactivity after ECT; in $\frac{1}{2}$ of the cases LSD brought about no changes. LSD intoxication occurred less frequently after ECT and produced less severe symptoms. No activating effect was observed.

Psychiatrische Universitätsklinik
Budapest, Hungary

2749 Karachutski, A.K. Eine Art rehabilitierende Therapie bei Geisteskranken, die mit Neuroleptika behandelt werden. [A kind of rehabilitation therapy for mentally ill patients treated with neuroleptic agents.] Psychiatrie, Neurologie und Med-

izinische Psychologie, 1962, 14, 377-381.

One-hundred-and-thirty-two patients who were hospitalized (most schizophrenics) were treated with neuroleptic agents. Sixty-six of these patients were, in addition, treated with physical therapy, while the other 77 patients were regarded as a control group. The age of the patients was 21-60 years; the average duration of psychotic illness $9\frac{1}{2}$ years. The neuroleptic drugs of choice were chiefly chlorpromazine, perphenazine and trifluoperazine [dosage unspecified]. The observation of the patients was focused on their psychopathological condition and was supported by a questionnaire completed by the patient, and the evaluation of "the acute effect" of the physical therapy. Rehabilitation is facilitated by physical therapy for the following reasons: 1/ it is a valuable tool for occupational therapy, 2/ the therapy per se has a rehabilitating effect, namely, physical and psychological rehabilitation and social and psychological rehabilitation and social adaptation and 3/ physiotherapy through its synergetic and complex action increases the therapeutic effect of neuroleptics and simultaneously prevents and alleviates side effects.

Wissenschaftliches Forschungsinstitut für
Neurologie und Psychiatrie
Sofia, Bulgaria

2750 Rosolleck, Horst, & Kunt, Turgut.
Über die Beeinflussung des postoperativen
Erbrechens. [The treatment of postopera-
tive vomiting.] Therapie der Gegenwart,
1962, 101, 325-328.

The antiemetic effect of Pervetral, 10-[3' (1- β -hydroxyethyl-4-piperazinyl)-propyl]-thiophenyl-pyridylamine, was investigated, and the postoperative vomiting occurring after general ether anesthesia compared in pretreated and control patients. Of 98 cases of the control series postoperative vomiting occurred in 60 patients. Two-hundred-and-fifty-one of the patients received Pervetral (25 mg i.m.) $\frac{1}{2}$ hours before the operation, in addition to the usual premedication. Vomiting occurred in 52 patients (20.7%) while 199 patients (79.3%) had no nausea or vomiting. In addition, a double-blind study was carried

out. At first, suppositories (30 mg) were used; the results were not satisfactory and 1 ml Pervetral (25 mg) or 1 ml of the placebo were administered. Pervetral was effective in 70%. The dosage was then increased according to age and condition (37.5-50 mg), and the results improved to 75-80%. In a further study, 21 patients with concussions (commotio cerebri) were treated with Pervetral. They received 25 mg at admission, regardless of whether vomiting had occurred or not. Nausea and retching could almost always be suppressed for 3-4 hours. Pervetral was well-tolerated, and has a sedating effect, potentiating the effect of analgesics.

Chirurgische Abteilung des Krankenhauses
Bethel
Bückeburg, Germany

2751 Thomas, Klaus. Suizidprophylaxe unter besonderer Berücksichtigung der pharmakopsychiatrischen Behandlung Lebensmüder. [Suicide prophylaxis with special consideration of the pharmaco-psychiatric treatment of depressed persons with suicidal tendencies.] Therapie der Gegenwart, 1962, 101, 319-321.

Suicides in Germany are almost as frequent as traffic deaths. This is a report on the activities of a medical agency which tries to cope with persons who want to take their own lives. It originated in 1956 in West-Berlin, and its telephones were used since that time by over 10,000 desperate and depressed persons. In cases of imminent suicide, hospitalization is attempted but often not possible. More often, the psychiatrists, physicians and social workers of the agency have to try to calm or treat the person in need. It was found to be an impossible task to cope with the anxieties, desperation, restlessness, affective tension and emotional lability without the help of drugs. A drug had to be found which was effective and could be used in visits without causing harmful side effects or severe hypnotic effects. The drug of choice was Phasein Forte (C.F. Boehringer, Mannheim), a combination of reserpine and orphenadrine. Twenty-five percent of all patients seen (2700 patients of whom 20% had endo-

genous and reactive depressions) received Phasein Forte, alone or in combination with reserpine or mephenamine (1st day: 1 tablet, increasing to 6-8 tablets; mg unspecified). After considerable improvement in psychopathological symptoms, the daily dosage was decreased by 1 tablet per week, until a maintenance dosage of 3 tablets daily was reached. Eighty-five percent of patients who took the medication consistently were markedly improved, and in most cases enabled to go on with their jobs.

Nismarckstrasse 66
Berlin-Steglitz, Germany

2752 Runyan, John W., Jr. Observations on the use of phendimetrazine, a new anorexi-
genic agent in obese diabetics. *Current
Therapeutic Research*, 1962, 4, 270-275.

Sixty of an original 76 diabetic patients completed a 3-month trial, 30 on phendimetrazine and 30 on placebo. The drug (35 mg tablets) was given 1/2 hour before each meal, as was placebo. Patients were not informed of the compounds anorexiogenic properties and the suggestive element in weight reduction was therefore minimized or eliminated. Phendimetrazine was found effective with negligible side effects (transient nausea in 5 and nervousness in 2). The weight loss on drug was 2.7 pounds compared to 0.91 pounds on placebo. (No refs.)

University of Tennessee
Division of Medicine
Memphis, Tenn.

2753 Chemotherapy Review. The treatment of psychoneurotic depressed patients with tranylcypromine/trifluoperazine, ('Parstelin'). Report of a general practitioner clinical trial conducted in Newcastle-on-Tyne. *Chemotherapy Review*, 1962, 2, 255-258.

Two-hundred-and-fifty-six patients suffering from depression with association of psychoneurotic states were treated with Parstelin (each tablet containing 1 mg trifluoperazine and 10 mg tranylcypromine). One tablet was usually given in the morning and early in the afternoon. On occasion 3

tablets a day were used. Of the 256 patients treated, results were satisfactory in 180, unsatisfactory in 76. In the 138 patients diagnosed as suffering from acute and chronic anxiety states with depression predominant, 91 responded satisfactorily but in 47 results were poor. In a group of 65 patients with endogenous depression response was good in 13. In the reactive depression group 12 out of 14 responded favorably. With a menopausal group of 25, 18 responded satisfactorily. Six out of 10 cases of involutional depression showed good response. Side-effects were negligible. (No refs.)

[No address]

2754 Schnetzler, J. P., Lamand, J. D., & Raynfeld, C. Un nouveau neuroleptique: la thioridazine. *Revue de la littérature. A propos de 110 cas traités.* [A new neuroleptic: thioridazine. Review of the literature on 110 treated cases.] *Journal de Médecine de Lyon*, 1962, 1010, 797-838.

Eighteen patients, 10 hebophenic, 4 paranoid 3 hebophreno-catatonia and 1 atypical depressive were treated with daily doses of 150-800 mg, average 420 mg/day for 2-6 months. In hebophrenia results were 6 marked improvements, 3 improvements and 1 failure. Four out of 4 paranoids improved markedly. The 1 case of hebophreno-catatonia decidedly improved and the 1 case of atypical depression showed improvement. Extrapyramidal signs were rare; hepatic and hemic toxicity absent as were allergies, however 1 case of pigmentary retinopathy occurred. One-hundred-and-eight references are appended.

Hôpital Psychiatrique de Saint-Egrève
Lyon, France

2755 Geller, E., Brill, N. Q., Crumpton, E., Eiduson, S., Liston, E., & Mizrahi, I. Adrenocortical activity in relation to the severity of schizophrenia. *Archives of General Psychiatry*, 1962, 6, 384-387.

Twenty male hospitalized schizophrenics, regressed and non-regressed (Disorganization Level Inventory & the Schizophrenic

scale from the Lorr Scales), were studied in relation to adrenal cortical activity using the urinary assay of 17-hydroxy-corticoids and 17-ketosteroids. Differences were found in the excretion of uric acid, inorganic phosphorus and 17-ketosteroids, but these are believed unrelated to adrenocortical activity. Adrenocortical activity was not directly related to the severity of illness.

Department of Psychiatry
UCLA Medical Center
Los Angeles, Calif.

2756 Schwartz, D. A. Paradoxical remission of psychosis. Archives of General Psychiatry, 1962, 6, 315-319.

The remission of 3 schizophrenics is discussed. In 3 of the cases tranquilizing medication (chlorpromazine up to 800 mg/day in 1 case and 600 mg chlorpromazine followed by 400 mg chlorpromazine plus 8 mg reserpine i.m.) was considered to be adjunctive and supportive to psychotherapy. Medication was not given long enough to determine its effectiveness. Also ECT was given in 1 case. Strong motivation for recovery and use of ego resources which the patient has not been utilizing are discussed.

Mental Health Services
Los Angeles County
Calif.

2757 Nölting, David E., Banal, Pio J., & Anguinetti, M. Nuestra experiencia con un nuevo psicofarmaco en el parto, el Ro-0690. [Our experience with a new psychopharmaka at delivery, Ro5-0690.] Prensa Médica Argentina, 1962, 49, 1767-1769.

Twenty-six primiparas, 14 secundiparas and 8 multiparas were given 100 mg or more of chloridazepoxide at delivery. In 9 cases 50 mg injections were used and also single 100 mg injections, but usually dosage was small. Anxiolytic and relaxing activity was found highly satisfactory. No respiratory depression of the mother or child was noted and the drug did not suppress the contractile activity of the uterus.

Ugarteche 2823
Buenos Aires, Argentina

2758 Duchastel, Yves. La methaqualone (methyl-2-orthotolyl-3 quinoxaline-4) HCl Hypnotique non barbiturique de synthèse (Etude clinique à "double inconnue" de 100 cas). [Methaqualone (methyl-2 orthotolyl-3 quinoxaline-4) HCl Synthetic non-barbiturate hypnotic ("double-blind" clinical study of 100 cases).] Union Médicale du Canada, 1962, 91, 288-290.

One-hundred patients, hospitalized for insomnia, were given 150 mg methaqualone or placebo at night on a double-blind basis. Eighty-seven % showed very good response compared to 46 % obtained with placebo. No physical side effects were noted.

Service de Neurologie
Hôtel-Dieu de Montréal
Montreal, Quebec
Canada

2759 Azima, H., Arthurs, Dorothy, Silver, A., & Azima, Fern J. The effect of MP-809 in depressive states: a multi-blind study. American Journal of Psychiatry, 1962, 119, 573-574.

MP-809, a tryptamine derivative, was investigated in 50 depressed patients and compared to 2 other groups of 50 depressed patients receiving inert and potent placebo in a multiple-blind study. The chemical formula is 4-methyl- α -methyl-tryptamine. The average daily dose was about 60 mg (20-100 mg) for an average period of 21 days and the potent placebo dose (phenobarbital) was 30 mg/day. Clinically MP-809 had a significant (marked to moderate) antidepressant action in 52 % of all patients and 74.1 % of neurotic depressions. Side effects were frequent but mild, consisting of fine hand tremors in 10 patients, drowsiness in 8, weakness in 6, dizziness in 5, fatigue in 4, nausea and vomiting in 5, generalized pruritis in 2, diarrhea in 2 and ankle edema in 1.

Department of Psychiatry
Psychopharmacology Section
Allan Memorial Institute
Montreal, Quebec, Canada

Clinical studies
Abstracts 2760-2763

2760 Bonhour, Alberto, Jones, Blanca, & Acebal, Enrique M. Experiencia clinica con fenelzina. [Clinical experience with phenelzine.] Prensa Médica Argentina, 1962 49, 2336-2341.

Twenty patients with manic-depressive psychosis, 7 with reactive depression, 5 neurotic depression, 3 involutional depression and 2 with depression emerging in the development of other psychoses were treated with 75 mg phenelzine/day in 32 cases and 45 mg/day in 5 cases for 30-40 days. Some dry mouth, orthostatic hypotension, paresis of the leg, etc. was noted. Manic depressives were treated with phenelzine and ECT. Out of 21 mental patients with manic psychosis, 12 remitted, 3 were improved and 6 showed no change of condition. Out of 6 cases of reactive depression 3 were in remission, 1 improved and 2 did not. Out of 5 cases of neurotic depression, 3 were in remission, and 2 had improved. With involutional depression 2 out of 3 were cured while the other remained unchanged. With psychotic depression neither of the 2 cases improved. Global results were 20/37 remission, 6/37 improvement and 11 no change.

Facultad of Medicina
Instituto de Clínica Psiquiátrica
Buenos Aires, Argentina

2761 Goldberg, Marshall. Thyroid impairment in chronic alcoholics. American Journal of Psychiatry, 1962, 119, 255-256.

Thyroid function was studied in 82 males and 18 females, aged 23-65 years, who were confirmed alcoholics. One or more baseline PBI determinations, the rise in the PBI 24 hours after 10 IU of thyrotropic hormone i.m., electrometric recordings of the Achilles tendon reflex by the Lawson kinemometer and the tanned red-cell agglutination procedure for the detection of circulating thyroglobulin antibodies were made. Forty-five of the 100 chronic alcoholics tested were found to be thyroid deficient to varying degrees, i.e., 47 considered euthyroid and the remaining 8 were placed in a "borderline hypothyroid" category. Among 47 patients considered frank or borderline hypothyroid and treated with thyroid hormone, 16 were lost to followup

thyroid hormone, 16 were lost to followup and the remaining 31 observed on treatment for a minimal period of 1 year. Twenty-four (77%) of the thyroid-treated patients seemed to derive considerable benefit from their returning to a euthyroid status.

Department of Medicine
University Hospitals
Madison 6, Wisc.

2762 Ban, T.A., & McGinnis, K. Comparative clinical study of two hypnotic drugs. Canadian Medical Association Journal, 1962; 87, 816-817.

The comparative sleep-inducing and sustaining effect of 0.5 g glutethimide and 0.5 g ethchlorvynol was studied in 20 hospitalized patients for 6 days in a double-blind crossover experiment. Ethchlorvynol was the most effective hypnotic. No side-effects were observed with either of the active medications or placebo.

Research Department
Verdun Protestant Hospital
6875 LaSalle Blvd.
Verdun, Quebec.
Canada

2763 Holmberg, Gunnar, Gershon, Samuel, & Beck, Lloyd H. Yohimbine as an autonomic test drug. Nature, 1962, 193, 1313-1314.

Fifteen male chronic schizophrenics and 9 normal volunteers were treated with up to 0.5 mg/kg yohimbine i.v. Findings were essentially the same for both groups. Autonomic and psychic changes were of the same type and extended over almost the same range. An increase in heart rate parallel to the degree of emotional reactivity. Yohimbine apparently produces stimulation of both sympathetic (rise in blood pressure, pupillary dilatation) and parasympathetic (flush, secretion of saliva and tears, gastrointestinal and bladder hypermotility) functions. Cause of erection, seen in a few of our subjects, was obscure. The psychic signs, simulating an anxiety reaction, together with the massive autonomic response seem to indicate an involvement of regula-

ry centres at the diencephalic level.

Ypsilanti State Hospital
Box A
Ypsilanti, Mich.

2764 Sparks, Robert D., Browne, Donovan
, & Ferrans, Victor, J. Thiethylperazine:
effect on postoperative vomiting and localiza-
tion in the central nervous system by
fluorescence technics. American Journal
of Gastroenterology, 1962, 37, 404-414.

In the 1st part of this study, 50 patients
received only placebo solution, 77 received
5 mg of a piperazine agent [unspecified]
and 83 received 10 mg thiethylperazine
i.m. The incidence of vomiting was 26% in
the placebo group, 16.9% in the "piperazine
agent group" and 8.4% in the thiethylpera-
zine group. The incidences of nausea for
these groups were 32, 27 and 17% re-
spectively. Then 119 postoperative patients
were given 20 mg thiethylperazine i.m. and
nausea recorded at 20% with vomiting at
1.4%, results which are comparable to
those in the double-blind study. In the 2nd
part, dogs were given 50-100 mg/kg thi-
ethylperazine i.v. in divided doses at 15-30-
minute intervals over a 1-2 hour period.
After the total dosage animals became
comatose but could be aroused by noise,
etc. The dogs were sacrificed 2-3 hours
after the beginning of the experiment.
Fluorescence localization established using fluo-
rescence microscopy was as follows (thi-
ethylperazine fluorescence): in the myelin
layers of the cerebellum, faint and diffuse
in the cerebral cortex, occasional spots in
central regions of the brainstem, in the
mucosal cells of the prepyloric gastric
mucosa, in parietal cells primarily, in the
fundic gastric mucosa, in the parenchymal
cells of the liver and in the tubular epithe-
lium (not in glomeruli) of the kidney. By
autoradiography and colometry the figures for
the cerebellum, cerebrum and brainstem
were: 202, 36 and 37 mg/g respectively.

Department of Medicine
Division of Gastroenterology
Louisiana State University School of Medicine
New Orleans, La.

2765 Sampson, Patsy Hallock, Ray, Thomas
S., Pugh, Lawrence A., & Clark, Mervin L.
Picture recognition as an index of social
sensitivity in chronic schizophrenia: the ef-
fects of chlorpromazine. Journal of Con-
sulting Psychology, 1962, 20, 510-514.

Picture recognition data were collected
from 72 chronic schizophrenic women on
chlorpromazine or placebo. Their ages
ranged from 28-53 years and they had been
hospitalized a minimum of 8 years. Fifty-
one were assigned to chlorpromazine and
21 to placebo. The treatments were admin-
istered double-blind for 10 weeks to a
maximal dose of 800 mg chlorpromazine
or 8 placebo capsules daily. A procedure
involving recognition of pictures of self
and others was devised and employed as a
measure of social sensitivity, social stim-
ulus value, and self acceptance. Chlorpro-
mazine produces increased social aware-
ness as measured by increases in both
nonverbal (sorting) scores and verbal (nam-
ing) scores. It produces a greater ac-
ceptance of selfimage as reflected in in-
creased frequency of acknowledgment of
own photographs. However no effect of
chlorpromazine on social stimulus value
was found.

Cornell University
Ithaca, N.Y.

2766 Horwitz, David, Fox, Samuel M. III,
& Goldberg, Leon I. Effects of dopamine
in man. Circulation Research, 1962, 10,
237-243.

Cardiovascular effects of dopamine in 11
normal volunteers and 2 patients undergoing
diagnostic cardiac catheterizations were
studied. Dopamine was prepared as a 1%
solution in saline and administered i.v.
Results of hemodynamic studies in 6 normal
subjects indicated that dopamine increased
cardiac output and stroke volume in all
subjects. Arterial pressure also increased
in all subjects with a predominant systolic
pressure increment. Calculated vascular
resistance decreased in 5 subjects and did
not change in the other subject. Changes
in heart rate were of small magnitude and
were inconstant in direction. Left arterial
pressure did not change in 2 patients at a

Clinical studies
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time when substantial increments in cardiac output were produced by dopamine. Comparison of the doses of dopamine and levarterenol calculated to produce equivalent increments in systolic pressure indicated that dopamine was 1/25 to 1/56 as potent as levarterenol in this respect.

National Heart Institute
Bethesda, Md.

2767 Dewar, Robert, & Ross, Hugo. The use and abuse of tranquillizing drugs for chronic mental patients. Canadian medical association Journal, 1962, 87, 1375-1377.

The behavior of 16 female hospitalized psychotic patients was measured while they received maintenance doses of chlorpromazine (average dose, 50 mg q.i.d.) and again while receiving identical doses of a placebo. The double-blind technique was employed. Nurses used a behavior rating scale to measure noisiness, personal cleanliness, interpersonal relations among patients, occupational activities, hostility, activity, cooperation, dress, eating and sleeping. Patients' behavior over a 6 week period of chlorpromazine administration was compared with behavior over an equal period of placebo administration. There was no evident difference in behavior in 90% of the cases. Among the others there was a slight trend towards improved behavior while the patients received placebo. Tranquillizing drugs are often used needlessly for chronic mental patients.

Psychology Department
McMaster University
Hamilton, Ontario
Canada

2768 Sibley, W.A., Tucker, H.J., & Randt, C.T. Quinacrine in the treatment of refractory petit-mal epilepsy. Canadian Medical Association Journal, 1962, 87, 6, [Abstract]

Thirty-three cases of petit-mal epilepsy were treated with atropine (Quinacrine) which successfully controlled seizures in 25 out of the 33. In 1 patient the seizures were suppressed for only 6 weeks, but in

the remainder the spells were controlled for long periods. Recommended dosage is 100 mg once a day p.o. Atropine does not influence grand-mal seizures. Only minor toxic effects were noted in 2 cases.

150 St. George Street
Toronto, Canada

2769 Tibbles, J.A.R., & Douglas, A. McGreal. Experience with a new anticonvulsant-U-7524. Canadian Medical Association Journal, 1962, 87, 1087, [Abstract]

Thirteen children with various forms of epilepsy were treated with U-7524 [dosage unspecified]. They were treated as inpatients for an average of 2 weeks. Treatment was continued for those who improved and subsequently 10 further patients were managed on an outpatient basis. Encouraging results were obtained.

[No address]

2770 Harding Le Riche, W., & Van Belle, Gerald. Study of phendimetrazine bitartrate as an appetite suppressant in relation to dosage, weight loss and side effects. Canadian Medical Association Journal, 1962, 87, 29-31.

The study was begun by randomly assigning 110 patients as they came to the office to schedules of 2, 3 or 4 tablets of phendimetrazine/day. When it became apparent that most people could tolerate 6 tablets daily, all subsequent patients were placed on this schedule. Tablets (35 mg) were taken t.i.d. or b.i.d. about an hour before meals. As the placebo effect on appetite suppression is negligible (Le Riche 1961), no placebo was used. Two, 3, or 4 tablets daily produced a weight loss of ca. 8 pounds compared with a loss of 12 pounds for those on the 6 tablet/day schedule. Minor side effects were common; a few patients developed glossitis and stomatitis which disappeared when medication was discontinued and recurred when it was resumed. A slight midriatic action of phendimetrazine was noticed in 5 patients. This action could be deleterious in patients with early glau-

ma if the diagnosis has not been previously recognized.

Department of Epidemiology
School of Hygiene
University of Toronto
Toronto Ontario
Canada

2771 Domínguez Lázaro, A.R., Sastre Castro, A., Pérez Guerrero, J., & Calleja Calas, J.L. El UML-491 (1-methyl d-lysergic acid butanolamide) en la profilaxis tratamiento de la jaqueca y otras cefalias. [UML-491 (1-methyl d-lysergic acid butanolamide) in the prophylaxis and treatment of migraine and other headaches.]

Eighteen cases of migraine headache, 1 case of Horden's headache and 3 other cases were treated with methysergide (UML-491), 3-8 mg/day in 3 divided doses for a total of 10-175 mg for 1-10 months. The general results of treatment were considered good though a longer control period and a larger caseload would be desirable for the determination of efficacy.

Clínica de Nuestra Señora de la Concepción
Madrid, Spain

2772 Duchastel, Yves. Methaqualone: a synthetic non-barbiturate hypnotic. A "double-blind" clinical evaluation of 100 cases. Canadian Medical Association Journal, 1962, 86: 586-587.

Methaqualone has been found to exert sedative and hypnotic effects which are in accord with previously published pharmacologic and clinical studies. A double-blind study on 100 patients showed that 87% of patients had a very good response compared to a 46% response obtained with a placebo. No appreciable side effects were noted.

Department of Neurology
Stel-Dieu
Montreal, Quebec
Canada

2773 Lawson, J.I. Murray, & McGowan, Stuart W. Haloperidol in obstetrics. A clinical trial in 350 women in labour.

Lancet, 1962, No. 7241, 1205-1208.

Haloperidol in a dose of 3 mg was combined with pethidine at usual clinical doses in the management of labor in 350 women, 50 of whom were injected i.v. while the remainder received haloperidol i.m. Sedation was deep after i.v. injection. The evidence suggested slowing of labor with a relatively high incidence of operative overdose. Bradycardia and hypotension occurred in some cases. Intravenous haloperidol is not advised for routine use in labor, but it may be useful in a minority of patients who need more sedation than usual injected i.m., haloperidol proved a safe and efficient complement to pethidine, providing good "psychic sedation", not interfering with the course of labor or causing fetal depression. There were no extrapyramidal, cardiovascular or other side-effects.

Department of Anesthetics
Royal Infirmary
Dundee, Great Britain

2774 Diggory, P. L. C., & Tomkinson, J. S. Nausea and vomiting in pregnancy. A trial of meclozine dihydrochloride with and without pyridoxine. Lancet, 1962, No. 7252, 370-372.

Of a random series of 100 pregnant women, 88 experienced nausea and vomiting; 73 had taken some form of medication, a large proportion treating themselves without any medical advice. In 23% of the affected patients the onset of vomiting preceded the 1st missed menstrual period and did not appear entirely psychosomatic. Meclozine is effective in the treatment of these cases. Twenty-five mg of meclozine was taken every morning and 50 mg at night, or placebo. Some received meclozine plus pyridoxine with the same dosage of meclozine used above, on a double-blind basis. Comparably good results were obtained with both active medications: 28 out of 41 on meclozine and 22 out of 35 on meclozine plus pyridoxine.

Queen Charlotte's Maternity Hospital
London W. 6, Great Britain

Clinical studies
Abstracts 2775-2778

2775 Bayliss, S.G., & Gilbertson, M.P. A trial of chlordiazepoxide in spastic children. *Lancet*, 1962, No. 7263, 995-996.

A double-blind, crossover trial with 41 spastic children was run in order to assess the value of chlordiazepoxide; however only 29 children completed the trial (1 had to be withdrawn because of side effects). Home rating and school rating showed a significant difference, but the psychotherapy and 6-ball test scores were not significant, which suggests that the improvement in the other ratings was due mainly to behavioral changes. Similar results could probably have been achieved with a sedative. Nineteen children did show signs of decreased spasticity or rigidity while receiving the drug, but 10 of these became too relaxed, resulting in less control and poorer posture. Side effects of drowsiness or increased irritability and aggressiveness were also troublesome. The dose of 0.75 mg/kg used is probably close to the upper limit of the tolerated dose.

Centre for Spastic Children
Chelsea, London, S.W. 3
Great Britain

2776 Aaronson, Herbert G., & Boger, William P. Incontinence in the elderly: an attempt at control. *Journal of the American Geriatric Society*, 1962, 10, 626-632.

Forty incontinent female patients (CBS, mental deficiency, involutional psychiatric reaction, manic depression reaction-manic type and schizophrenia) were given bedtime administration of either 25 mg imipramine or matching placebo. Each patient served as their own control. Most patients were past 60 years of age. No benefit was obtained from imipramine or placebo in relation to incontinence. Nevertheless the moral of the patients was notably increased, apparently due to a program which brought together the attendant, nursing and medical personnel in a shared therapeutic effort.

Arthur P. Noyes Research Department
Norristown State Hospital
Norristown, Penna.

2777 Simpson, George M., & Harris, Albert H. The effect of tri-iodothyronine on abnormalities in the cerebrospinal fluid of chronic schizophrenic patients. *American Journal of Psychiatry*, 1962, 119, 170-171.

Proteins were obtained from 26 chronic schizophrenics and gold curves on 27. The protein level previous to triiodothyronine treatment (25 mcg triiodothyronine/day increased every 2 weeks by 25 mg to the level of 100 mcg/day, maintained for 45 days) was 39 mg% (upper limit of normality 40%) and after the course of triiodothyronine, 30 mg%. Previous to treatment 10 patients had a value above 40 mg% and post treatment only 4 patients had had a level above 40 mg%. Of the 27 gold curves, 8 were reported as normal, 8 slightly abnormal and 11 markedly abnormal pretreatment. Following treatment 13 were normal, 10 slightly abnormal and only 4 markedly abnormal. Decrease metabolism is presumed to be a relating factor.

Rockland State Hospital
Rockland, N. Y.

2778 Mandel, William, & Evans, Philip. Comparison of butyrylperazine and trifluoperazine in chronic schizophrenic subjects. *American Journal of Psychiatry*, 1962, 119, 70-72.

A double-blind crossover study with fixed dosage regimens and 2 placebo intervals was conducted with 44 hospitalized chronic schizophrenic males. The dosage of butyrylperazine was 10 mg t.i.d. and of trifluoperazine 8 mg t.i.d. and the treatment period 3 months. There were no significant differences in therapeutic effectiveness or incidence of side effects between the 2 drugs. The overall rating of improvement after 4 weeks was: butyrylperazine marked improvement 14%, moderate 10% and slight 38%, and trifluoperazine *ibid.*, 14%, 20% and 33%.

Napa State Hospital
Napa, Calif.

See Also 2552, 2568, 2573, 2617, 2622, 2631, 2632, 2633, 2634, 2635, 2789, 2

SIDE EFFECTS

2779 Lenz, W., & Knapp, K. Foetal malformations due to thalidomide. German Medical Monthly, 1962, 7, 253-258.

greatly increased incidence of certain congenital anomalies, particularly phocomelia, was noted in 1961 in many parts of Germany and other countries. In Hamburg the incidence of such congenital anomalies was 0.17% of all newborns while that of other types of congenital anomalies had not changed. Retrospective inquiry has shown that most mothers of children with the newly observed types of embryopathy (phocomelia) had taken thalidomide or thalidomide-containing drugs during the early months of pregnancy. In 1/2 of the cases only the arms have been involved, in 1/4 the cases arms and legs, while absence of ears occurred in 1/6 of the cases. The critical phase of toxic thalidomide action has been found to be between the 27th and 30th day after conception.

Universitäts-Kinderklinik
Martinistr. 52
Hamburg-Eppendorf, Germany

2780 Shaw, F.H. A clinical and experimental study of bromide intoxication, with special reference to bromureides. Medical Journal of Australia, 1962, 1, 421-422. [letter]

While agreeing that inorganic bromides have no place in modern medicine, a plea is entered for the continued use of bromureides.

University of Melbourne
Parkville, Victoria, Australia

2781 Coodin, Fischel J., Uchida, Irene A., Murphy, Claude H. Phocomelia: report of three cases. Canadian Medical Association Journal, 1962, 87, 735-739.

Three infants were born with phocomelia in Winnipeg, Canada during the period May 1961 to May 1962. In 1 case thalidomide had been administered to the mother early in the pregnancy. No etiological agent was discovered in the other 2 cases, both of whom died. Known teratogenic agents

able of causing phocomelia are reviewed.

Department of Pediatrics
University of Manitoba
Canada

2782 Easson, William M. Gasoline addiction in children. Pediatrics, 1962, 29, 250-254.

An 11-year-old and a 14-year-old boy, both mentally disturbed, were hospitalized because of gasoline sniffing. These boys were able to tolerate gasoline inhalation over prolonged periods, sometimes for several hours without physical discomfort which might indicate a degree of physical tolerance. No specific withdrawal reaction was noted.

Children's Service
Menninger Clinic
Topeka, Kan.

2783 Ling, George M., Dolman, C.L., & Boyd, John R. Drug-induced (thalidomide) malformations. Canadian Medical Association Journal, 1962, 87, 1259-1262.

Two cases of infants born with phocomelia, amelia and alimentary abnormalities are presented, where the mothers had received thalidomide in early pregnancies. The question is raised whether or not similar abnormalities might occur in comparable circumstances after the administration of other glutarimides currently in clinical use. Drug therapy should be kept at a minimum in pregnancy, particularly the first trimester.

Department of Pharmacology
Faculty of Medicine
University of British Columbia
Vancouver, British Columbia
Canada

2784 Le Van, Paul, & Bierman, Stanley M. Idiosyncratic drug eruption to Dilantin and trimethadione. Archives of Dermatology, 1962, 86, 254-256.

A 16-year-old boy developed a spontaneous

Side effects
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akinetic seizure and was placed on diphenylhydantoin (Dilantin, 100 mg t.i.d.) and 3 weeks later developed a pruritic morbilliform eruption of his trunk, low-grade fever, nausea and sore throat. Three weeks later the patient was placed on trimethadione, 300 mg t.i.d. and a month later developed photophobia, butterfly facial eruption, fever and malaise and was readmitted to the hospital. All antiepileptic agents were withdrawn and the patient improved on 30 mg prednisone.

[No address]

2785 Pisciotta, Anthony V., & Kaldahl, Joyce. Studies on agranulocytosis. IV. Effects of chlorpromazine on nucleic acid synthesis of bone marrow cells in vitro. Blood Journal of Hematology, 1962, 20, 364-376.

Studies were conducted on the bone marrow of 27 random hospital patients who had never received chlorpromazine and therefore were not known to be sensitive to this drug. Also similar studies relating to solutions of chlorpromazine on incorporation of H^3 -thymidine and uridine were performed on the bone marrow of 5 men and 4 women who had had agranulocytosis following treatment with chlorpromazine and were now recovered. These results were compared to those obtained from 10 persons who had been treated with comparable doses for more than 2 months without developing agranulocytosis and 12 randomized hospital patients who had never received chlorpromazine. When viable marrow cells were incubated with tritiated thymidine and uridine, the cells became radioactive as nucleic acid synthesis proceeded. Excessive concentrations of chlorpromazine partially inhibited the influx of thymidine and uridine into granulocytes of all patients who had had agranulocytosis due to this drug, and of about 75% of random hospital patients. This drug did not effect nucleic acid synthesis in nine individuals who had been treated with a large amount of chlorpromazine, with no alteration in their leukocyte count. A comparison of the effects of dilution of chlorpromazine upon influx of H^3 -thymidine into granulocytes showed significant dose-de-

pendent depression of granulocyte labeling in chlorpromazine-sensitive persons, and no depression in granulocytes of persons on large doses of chlorpromazine who did not develop leukopenia. Random hospital patients not on chlorpromazine showed degree of depression between these two groups. The number of radioactive normoblasts in the marrow culture preparation diminished slightly, but not significantly following incubation with chlorpromazine. Nonmyelotoxic drugs, i.e., penicillin, acetylsalicylic acid has no significant effect on the degree of influx on tritiated thymidine and uridine. Chlorpromazine had no effect on the incorporation of radioactive DL-leucine into marrow cells.

Marquette University School of Medicine
Marquette, Wisc.

2786 Warpechowski, Bernard. Neurological symptoms in children in severe accidental poisoning with chlorpromazine. Pediatrica Polonica, 1962, 37, 1311-1315.

An increasing number of accidental poisonings in children is occurring with phenothiazine derivatives because of their wide use. Twelve acute accidental poisonings of children with chlorpromazine are reported. CNS symptoms are most prominent. In spite of the severity of cases children usually survive with good nursing care and symptoms disappear after several days. As death might result, all children so poisoned should be hospitalized.

Wojewodzki Szpital Dzieci
Poznan, Poland

See also 2553, 2562, 2565, 2585, 2586, 2605, 2636, 2671, 2690, 2698, 2714

BEHAVIORAL STUDIES

2787 Linton, Harriet B., & Langs, Robert. Subjective reactions to lysergic acid diethylamide (LSD-25). *Archives of General Psychiatry*, 1962, 6, 352-368.

Thirty subjects were given 100 µg LSD orally and 20 given a placebo, on a double-blind basis. A 47-part questionnaire was applied 7 times: on the pretest day, 1/2 hour after administration, 2, 5 and 8 hours, and the posttest day as well as retrospective testing, made immediately after the posttest questionnaire. The LSD group suffered from difficulty in thinking and the control of the flow of thoughts, reporting impairment in thought processes, judgement and concentration, loss of control over thoughts and had feelings of tension. Symptoms of numbness, feeling cold or hot, nausea, feeling physically weak and finding difficulty to move as well as distortions in perception (loss of time sense and reality contact, etc.) were also noted. Three distinct reaction patterns occurred: 1st group reported primarily a loss of control, elation and vivid imagery with perceptual distortions, another group reported striking changes in thought image, including body image, and thought that they had learned something about themselves from the experience, while the 3rd group reported great fear of losing control and automatic symptoms.

Psychiatric Research Center for Mental Health,
New York University
New York, N.Y.

2788 Feldman, Robert S., & Lewis, Everett. Response differences of psychotropic drugs in rats during chronic anxiety states. *Journal of Neuropsychiatry*. 1962, 3, 527-541.

Rats were trained to respond to a Lashley jumping apparatus (in front of two stimulus windows): left or right, bright or dark). Comparisons were made among drug- and electroshock-treated rats with respect to anxiety prevention. Evaluation of the following drugs was made during insoluble and insoluble problems: 0.20 mg/kg and 0.40 mg/kg reserpine, 5.0 mg/kg chlorpromazine, 80 mg/kg meprobamate, 25mg/kg phenobarbital, 1.75 mg/kg dexamphet-

amine, 3.0 mg/kg iproniazid, 35-37.5 mg/kg phenelzine, 1.2 g/kg alcohol, 15 mg chlordiazepoxide and 3 mg/kg diazepam. The action of chlordiazepoxide differed from that of the other drugs, probably through quantitative fear reduction. The method appears to be a step forward towards the goal of specifying the mechanism of abnormal behavior, and aid in the establishment of methods of reliable drug assessment.

University of Massachusetts
Amherst, Mass.

2789 Hoffer, A. Lack of potentiation by chlordiazepoxide (Librium) of depression or excitation due to alcohol. *Canadian Medical Association Journal* 1962, 87, 920-921.

A double-blind study was conducted comparing the interaction of 10 mg chlordiazepoxide for 1 day and 6 ounces of rye whiskey given over a 3-hour period in the evening of the same day. The comparison drug was a placebo. Four evening experiments were conducted using the same 6 normal subjects and 2 observers. At the end of the evening, the observers were unable to detect which subjects had had placebo or chlordiazepoxide. Therefore the recommended therapeutic dose of chlordiazepoxide did not potentiate what was considered a social quantity of alcohol.

Psychiatric Research Branch
University Hospital
Saskatoon, Saskatchewan
Canada

2790 Savage, R.D. The effect of reserpine on conditioned fear responses. *British Journal of Psychology*, 1962, 53, 451-454.

Eight naive kids were placed in a harness with electrodes fastened to the right foreleg. The feared stimulation was an US of 10 volts inducing specific learning of a flexion response. A continuous 2-second electric shock was presented to the foreleg. Drug dosages (mg/lb) were 0.125 saline; 0.0375, 0.625 and 0.125 reserpine. Foreleg flexion and ambulation response showed that as the drug dosage increased

the flexion scores increased ambulation decreased. This lowering of general activity could be related to drug effect on the limbic, hypothalamic and reticular systems, or a general decrease in motor facility because of depressant effect.

University of New England
Australia

- 2791 Ray, Oakley S., & Marrazzi, Amedeo S. Interaction of reinforcement schedule and dosage on response rate changes following drug administration. *American Psychologist*, 1962, 17, 397. [Abstract]

Food- or water-deprived rats were tested in a single session on both a fixed ration and a DRL schedule using separate levers and tones as discriminative stimuli. Amphetamine (0.25-4.0 mg/kg) was administered just before the start of the run. Three patterns of responding were obtained: at low doses response rates on both schedules increased; at moderate levels rates increased further on the DRL schedule and were depressed on the FR schedule; at higher doses rates on both schedules were depressed. The effects of amphetamine are dependent on both dose and behavioral procedure and all the above effects can be determined by 1 CNS effect that is dose dependent and results in a loss of control by the animal.

VA Research Laboratories in Neuropsychiatry
Pittsburgh, Pa.

- 2792 Oken, Donald, Grinker, Roy R., Heath, Helen A., Herz, Marvin, Korchin, Sheldon J., Sabshin, Melvin, & Schwartz, Neena B. Relation of physiological response to affect expression. Including studies of autonomic response specificity. *Archives of General Psychiatry*, 1962, 6, 336-351.

The physiological and psychological stress responses of 18 normal college students were studied with the primary purpose of testing the hypothesis that limitation of affective expression (lack of "discharge") under stress is associated with heightened physiological response. Two groups of 9

subjects each were selected on the basis of interview ratings, to represent opposite ends of the continuum of affective lability range and threshold. Measurements of physiological variables and ratings of psychiatric response categories (3 affective and 3 defensive), including the Adjective Check List, Stroop test, Norolis Mood scale and Nandler Perception Questionnaire, were made during 3 experimental afternoon sessions 1 week apart. The initial day embodied psychologically stressful stimuli consisting of the alleged administration of a dangerous psychoactive drug and the viewing of a film of mutilative surgery in a setting of maximum ambiguity and lack of support. The 2nd day stress was high heat (95 F) and humidity (50%). The 3rd day was used to obtain control measures. Stress responses occurred generally as anticipated for both types of stimuli. The psychological stress produced the greatest affective and defensive stimulation and there was little arousal on the control day. Physiological responses differed on the 2 days in a manner related to the nature of the stimuli: the affectively expressive ("high") group had significantly greater psychological response than the more constrained ("low"). The hypothesis that the affectively less expressive subjects would manifest greater physiological response generally was not substantiated. Autonomic response specificity does seem to characterize individuals, it largely characterizes their tendency to maintain a stable hierarchy of level rather than a consistent pattern of change.

Institute for Psychosomatic and Psychiatric Research
29th Street and Ellis Avenue
Chicago 16, Ill.

- 2793 Werboff, Jack, & Havlena, Joan. Post-natal behavioral effects of tranquilizers administered to the gravid rat. *Experimental Neurology*, 1962, 6, 262-269.

Gravid rats received daily dosages of 0.1 mg/kg reserpine, 6 mg/kg chlorpromazine, 60 mg/kg meprobamate s.c. or a control injection of distilled water during 1 trimester of gestation on days 5-8, 11-14 or 17-20. Administration of tranquilizers to

the gravid animal resulted in behavioral alterations that persisted through adulthood. Evaluation of activity level on the inclined plane test at 25 days of age showed that the offspring of all drug-treated mothers were less active than control offspring. A similar decrease in activity and emotionality, as measured by responses in the open field test, was further observed when the animals were 55 days of age. Audiogenic seizure susceptibility, tested at 120 days of age, showed that the drug group offspring were more resistant to stimuli than the control offspring. Behavioral effects result from the administration of tranquilizers to the gravid animal and were independent of the trimester of gestation and pharmacological differences among the drugs.

Animal Behavior Laboratory
Lafayette Clinic
Detroit, Mich.

2794 Scheckel, Carl L. Effects of chlorpromazine and chlordiazepoxide on delayed matching in the monkey as measured by a self-adjusting procedure. *American Psychologist*, 1962, 17, 398. [Abstract]

Monkeys trained on an automatically controlled, delayed matching schedule were tested under several doses of chlorpromazine, 0.31 to 1.0 mg/kg and chlordiazepoxide 0.156 to 40 mg/kg. The delay intervals which could be presented to the subjects extended from 1 to 105 seconds, but the particular delays presented in any session were a function of the subject's responses, and were programed on a self-adjusting schedule. By this procedure correct matching responses increased the delay on successive trials, and incorrect responses decreased the delay; thus allowing the subject to determine its own limit of delay under drugged and nondrugged conditions. Large doses of chlorpromazine and chlordiazepoxide produced significant decreases in the limit for all subjects. Smaller doses of chlorpromazine produced a slight increase in the limit in 1 subject, and moderate doses of chlordiazepoxide produced significant increases in the limit of delay for all subjects.

Hoffmann-La Roche, Inc.
Nutley 10, N.J.

2795 Leaf, Russell C. Discriminative classical conditioning under curare can control the performance of subsequently learned avoidance responses. *American Psychologist*, 1962, 17, 398. [Abstract]

Dogs were completely immobilized by injections of d-tubocurarine. While paralyzed, they were given discriminative fear conditioning to 2 tones; 1 tone was consistently reinforced with shock presentations while the other was never reinforced. After recovery from paralysis, subjects were never reinforced. After recovery from paralysis, subjects were given avoidance training in which visual stimuli were used as conditioning stimuli. This was given in the same apparatus in which classical conditioning occurred, or in a different apparatus. Results obtained during extinction testing showed consistent discriminative transfer of both types of avoidance response in both situations by all subjects.

University of Pennsylvania
Philadelphia 4, Pa.

2796 Gardner, Lucy, & McCollough, Celeste. A reinvestigation of the dissociative effect of curare-form drugs. *American Psychologist*, 1962, 17, 398. [Abstract]

Recent experiments employing the curare-form drug d-tubocurarine have produced results contradictory to those reported for earlier experiments which employed curare-form drugs, with respect to their "dissociative" effect on transfer of learning from drug to normal state and vice versa. The present experiments support the data on the dissociative effect of erythroidine (which, pharmacologically, differs considerably from raw curare) and the failure of d-tubocurarine to produce dissociation (though pharmacologically very similar to raw curare). Atropine blocked the erythroidine effect. Effects of the 2 curare-form drugs on autonomic and striate muscle conditioning were measured in both classical and avoidance conditioning situations.

Oberlin College
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See also 2579, 2586, 2619, 2621, 2642, 2650, 2765, 2767

2797 Necina, J. Antagonism between L- α -methyl DOPA and reserpine. *Life Sciences*, 1962, 2, 301-303.

Female Wistar rats and female mice were used in the following tests: cataleptic reaction, ptosis, pentetrazol tonic seizure threshold, cholesterol level in adrenals and adrenal ascorbic acid determination. One group of animals was given 400 mg/kg α -methyl DOPA i.p. followed 2 hours later by 5 mg/kg reserpine i.p. The 2nd group was given saline instead of α -methyl DOPA, while in the 3rd group reserpine was replaced by saline. The 4th group was treated twice with saline only. With reserpine only, all animals showed marked ptosis and catalepsy, while in the α -methyl DOPA group only a marked degree of ptosis was observed. The threshold of pentetrazol tonic seizure was decreased in only the reserpine treated group. An analogous inhibition of reserpine effect was apparent in rats, where α -methyl DOPA inhibited reserpine-induced depletion of adrenal cholesterol and ascorbic acid completely.

Research Institute for Natural Drugs
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2798 Costa, E., Gessa, G.L., & Brodie, B.B. Influence of hypothermia on chlorpromazine-induced changes in brain amine levels. *Life Sciences*, 1962, 2, 315-319.

Chlorpromazine (20 mg/kg i.p.) administered to normal rats did not change the brain content of 5HT and levarterenol, but as described by others, markedly antagonized reserpine in liberating amines from their storage sites. As this dose of drug reduced body temperature by about 8°C, role of this hypothermia in blocking amine depletion through repetition of the studies in rats maintained at an environmental temperature of 35°C was investigated. Chlorpromazine no longer produced hypothermia, nor did it inhibit the reserpine-induced drop in brain amines. Further evidence that the inhibition of amine release was a hypothermic effect was obtained by studies of the influence of chlorpromazine on amine depletion elicited by SU9064 and tetra-*benazine*, reversibly-acting reserpine-like

drugs. These drugs act on the same sites as reserpine but elicit pharmacologic responses and changes in brain amines that are short-lived and temporally related to the presence of drug in the brain. Chlorpromazine did not prevent these reversibly-acting drugs from releasing amines. The bonding of reserpine with storage receptors probably involves a reaction highly sensitive to temperature changes, whereas the bonding of the reversibly-acting drugs is relatively independent of temperature.

Laboratory of Chemical Pharmacology
National Heart Institute
Bethesda 14, Md.

2799 Brown, D.A. An eserine-like action of chloral hydrate. *British Journal of Pharmacology*, 1962, 19, 111-119.

The i.a. injection of chloral hydrate potentiated the transmissions of nerve impulses through the cat superior cervical ganglion, antagonized the ganglion-blocking action of hexamethonium, and greatly enhanced the ganglion-stimulant action of acetylcholine. Effects on the ganglion-stimulant actions of carbachol, nicotine, tetramethylammonium and potassium chloride were slight or absent and chloral hydrate itself usually did not stimulate. The neuromuscular-blocking action of tubocurarine on isolated rat diaphragm was completely and rapidly reversed by chloral hydrate. This reversal was prevented by previous neostigmine treatment. Chloral hydrate potentiated acetylcholine and nicotine effects on isolated rabbit duodenum and over 1 mg/ml produced a spasm.

St. Bartholomew's Hospital
London, Great Britain

2800 Kono, Chikao, Kanda, Zengo, Sekiya, Atsushi, & Saji, Eizo. Effects of monoamine oxidase inhibitors on the vasopressor actions of several sympathomimetic agents. *Nagoya Journal of Medical Science*, 1962, 24, 159-170.

Pheniprazine and phenelzine were studied in conjunction with epinephrine, tetrahydrozoline, ephedrine, tyramine, acetylcholine and heptaminol monophosphate in rabbits. The actions of ephedrine and tetrahydrozoline on arterial pressure were significantly

reduced by both inhibitors. This reduction may be closely related to MAO inhibition. The actions of epinephrine and heptaminol were not significantly altered by the administration of the inhibitors. The nicotinelike action of acetylcholine was not blocked by pheniprazine and therefore the release of catecholamine may not be reduced by small doses of this inhibitor.

Department of Pharmacology
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Nagoya, Japan

2801 Trendelenburg, U., Muskus, A., Fleming, W.W., & Gomez Alonso de la Sierra, B. Effect of cocaine, denervation and decentralization on the response of the nictitating membrane to various sympathomimetic amines. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 181-193.

Dose-response curves of 14 sympathomimetic amines were studied on the nictitating membrane of spinal cats. Some of these amines had only direct effects, e.g., levarterenol, some had only indirect effects, e.g., tyramine, while others had both direct and indirect actions, e.g., ephedrine. Cocaine antagonized all indirect effects of tyramine- and of ephedrinelike amines. The well known sensitizing effect of cocaine was found to be very pronounced with all compounds which, as a characteristic structural feature, possessed a phenolic hydroxyl group in the meta-position; the para-OH analogues and the corresponding parent compounds with no phenolic hydroxyl groups were much less or not at all potentiated by cocaine, even when these amines had direct actions. Hence the sensitizing action of cocaine is more specific than heretofor assumed. Decentralization, on the other hand, caused supersensitivity to all amines with direct, mixed or indirect actions. This supersensitivity, which was studied with 9 amines, was of an equivalent magnitude for all. The effect of denervation of the animal was very similar to that of cocaine, but certain differences were also observed. It is proposed that the effect of denervation is best described as corresponding to the sum of the effects of cocaine, of decentralization and of depletion of the levarterenol stores.

Department of Pharmacology
Harvard Medical School
Boston, Mass.

2802 Wiseman, Ralph, Jr. The effect of acute and chronic administration of chlorpromazine on the I^{131} distribution in normal rats. *Journal of Pharmacology and Experimental Therapy*, 1962, 138, 269-276.

Adult male Sprague-Dawley rats were given 25 mg/kg chlorpromazine i.p., followed immediately by 30 mg/kg water by oral intubation to facilitate diuresis during the subsequent 6-hour test period. After 30 minutes animals were anesthetized and given ca 6 μ c of sodium iodide- I^{131} i.v. Total urine and the thyroid gland tissue were assayed. In a 2nd series fasted rats were used. In chronic experiments rats received 1 mg/kg chlorpromazine daily and 6-hour I^{131} distributions were assayed at 35, 62 and 89 days. Blood pressure studies were made in an additional group of rats. After a single i.p. dose of 25 mg/kg of body weight of chlorpromazine in the rat a 40.3% decrease in the 6-hour I^{131} uptake by the thyroid was observed. Other changes encountered in these animals in 6 hours were a 92.7% decrease in urinary excretion of I^{131} , 29.7% increased retention of I^{131} in the body and 58.0% reduction in urine volume. Sixty-six hours after the last dose, the 6-hour I^{131} uptake was decreased 40.4%.

Radioisotope Service
VA Medical Teaching Group Hospital
Memphis, Tenn.

2803 Camponovo, Luis Emilio, & Langer, Salomon Z. Acción de la diethylamida del ácido vanilínico sobre una cepa de ratones refractarios al estímulo audiogénico. [The action of vanilic acid diethylamide on a strain of rats refractory to audiogenic stimulus.] *Prensa Médica Argentina*, 1962, 49, 1414-1418.

Young C_3H/Ep rats were divided into 4 groups and studied as followed: controls, 10 mg/kg, 20 mg/kg and 30 mg/kg s.c. vanilic acid diethylamide. They were exposed to audiogenic stimuli once a day for

5 days and graded: jumping, flight, convulsions, catatonia and death. The drug sensitized the animals in proportion to dose, as well as causing proportional decrease in the latency period responses. A death rate of ca. 75% was obtained with 30 mg/kg. The 2 values obtained were: controls 0, 10 mg/kg 9.13, 20 mg/kg 36.25 and 30 mg/kg 39.47.

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Buenos Aires, Argentina

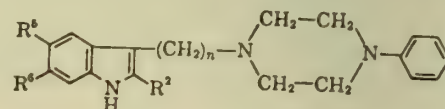
2804 Drakontides, A.B., Schneider, J.A., & Funderburk, W.H. Some effects of sodium gamma-hydroxybutyrate on the central nervous system. *Journal of Pharmacology and Experimental Therapy*, 1962, 135, 275-284.

Behavioral studies in cats and mice and EEG investigations in cats indicate that sodium γ -hydroxybutyrate by i.v., i.p. and oral routes is a CNS depressant with a characteristic dose-dependent spectrum of activity, and a very low order of toxicity. In doses of 100 mg/kg and higher, decreased responsiveness to optic, acoustic and pain stimuli, drowsiness associated with ataxia, decreased spontaneous motor activity, muscular flaccidity and a state of detachment from environmental conditions were observed. In accord with the behavioral findings, EEG studies indicated slowing of electrical brain activity, decreased responsiveness of the reticular activating system to electrical stimuli, enhancement of thalamo-cortical recruitment and a trend toward prolongation of induced seizure activity of the limbic system. The effects of this drug could be readily differentiated from those of known sedatives, hypnotics and tranquilizers.

Department of Macrobiology
Medical Research Laboratories
Charles Pfizer & Co., Inc.
Groton, Conn.

2805 Wylie, David W., & Archer, S. Structure-activity relationships of 1-[(3-indolyl)alkyl]-4-arylpiperazines. A new series of tranquilizers. *Journal of Medicine and Pharmaceutical Chemistry*, 1962, 5, 932-943.

Compounds of a series of indolylalkylphenylpiperazines have been found active as CNS depressants (potentiation of hexobarbital anesthesia, head-withdrawal reflex, adrenergic blocking activity). The basic structure for CNS depressive activity was found to be:



Although these agents possess peripheral adrenolytic activity to the same degree as phenothiazines and benzodioxanes, no definite correlation could be found between various central activities and peripheral adrenolytic activity.

Departments of Pharmacology and
Chemistry
Sterling-Winthrop Research Institute
Rensselaer, N.Y.

2806 Bonnycastle, D.D., Bonnycastle, M.F., & Anderson, E.G. The effect of a number of central depressant drugs upon brain 5-hydroxytryptamine levels in the rat. *Journal of Pharmacology and Experimental Therapy* 1962, 135, 17-20.

Male Sprague-Dawley rat cerebral 5HT content after the i.p. administration of drugs was bioassayed using heart tissue from commercial oysters (*Venus mercenaria*). Corroborative fluorimetric determinations were also carried out. A variety of central depressant drugs, including sedatives (mostly barbiturates), hypnotics, analgesics, fixed and volatile anesthetics, during the course of their pharmacologic action result in a significant elevation of cerebral 5HT. Similar increases in brain 5HT have been detected following treatment of rats with pentobarbital, chloral hydrate, diphenylhydantoin and harmaline.

Department of Pharmacology
Seton Hall college of Medicine and
Dentistry
Jersey City, N.J.

2807 Brodie, B.B., Gessa, G.L., & Costa, K. Association between reserpine syndrome and blockade of brain serotonin storage

processes. Life Sciences, 1962, 2, 551-560.

Experiments were carried out with male adult New Zealand White rabbits and male adult NIH general purpose mice. α -Methyl-metatyrosine, Su 9064 (Methyl ether of methyl reserpate), reserpine and tetrabenazine were studied in relation to catacholimine depletion and blockade. Levarterenol 5HT, dopamine and the total decarboxylated products of α -methyl-metatyrosine were assayed. In mice and rabbits pretreated with α -methyl-metatyrosine to deplete the brain of catacholimes, the pharmacologic activity elicited by reserpine was closely correlated with inhibition of 5HT storage. Three different types of reserpinelike drugs produced pharmacological activities closely related to the extent of blockade of 5HT storage. Time-course responses also indicate that reserpine action is related to the impairment of 5HT storage.

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2808 Bertaccini, G., & Erspamer, V. The effect of the administration of water or isotonic NaCl solution on the urinary excretion of 5-hydroxyindoleacetic acid in the rat. Journal of Pharmacy and Pharmacology, 1962, 14, 687-697.

Administration of tap water by stomach tube or of isotonic saline orally or s.c. produces a conspicuous increase in the urinary excretion of 5HIAA in the rat. The same increase can be observed after administration of water plus posterior-pituitary antidiuretic hormone (ADH). Tap water is less effective than saline while the latter is more effective by the s.c. route than by mouth. Increase of 5HIAA may be, for short periods, as high as 3 times normal. The minimum oral dose of tap water causing a significant increase in urinary 5HIAA is 2 ml/100 g, that of saline produce a more intense and long-lasting increase of 5HIAA output than single doses. Generally, excess 5HIAA coincides with excess urine elimination, but there is no obligatory correlation of the intensity

of the two phenomena. Recovery, as urinary 5HIAA, of exogenous 5HIA, 5HT and 5HPT is the same in control, nonhydrated rats and in rats given single or repeated doses of tap water, tap water plus ADH, or isotonic saline. The mechanism by which water or saline administration produces increased urinary excretion of 5HIAA is discussed.

Institute of Pharmacology
University of Parma
Parma, Italy

2809 James, J.A., Kimbell, Lewis, & Read, William T. Experimental salicylate intoxication I. Comparison of exchange transfusion, intermittent peritoneal lavage, and hemodialysis as means for removing salicylate. Pediatrics, 1962, 29, 442-447.

Fasting dogs were given 125 mg/kg salicylate i.v. Following an equilibrium period (usually 1-2 hours), the selected procedure was begun under pentobarbital anesthesia and was continued for 4 hours, i.e., exchange transfusion, peritoneal lavage, hemodialysis. All animals developed some hyperpnea following administration of salicylate, but other symptoms of intoxication did not appear. Hemodialysis with albumin was the most efficient method of removing salicylate, about 50% of the dose being removed during the 4-hour period. Exchange transfusion and peritoneal lavage were considerably less efficient. Peritoneal lavage with 5% albumin solution was more effective than lavage with an equal conventional dialysis solution, but absorption of albumin from the peritoneum took place unless addition dextrose was added to the solution. The amount of salicylate excreted in the urine sometimes exceeded that removed by peritoneal dialysis or exchange transfusion.

Department of Pediatrics
University of Texas Southwestern Medical School
Dallas, Texas

2810 Hilton, James G. A proposed mechanism for epinephrine potentiation by ganglionic blocking agents. American Journal of Physiology, 1962, 203, 753-757.

The blood pressure responses elicited in dogs by the injection of 1.0, 5.0, and 10.0 $\mu\text{g/kg}$ of epinephrine were studied before and after blockade of autonomic nervous activity by either ganglionic blocking agents or by total spinal anesthesia. After blockade, blood pressure levels of 100, 130 and 160 mm Hg were maintained by infusion of epinephrine. The pressor responses elicited were inversely related to the level of the maintained blood pressure and the maximal attained blood pressures did not change markedly with the various maintained blood pressures. In a series of animals treated with ganglionic blocking agents, (procaine or chlorisondamine dimethochloride), the maximal blood pressures were approximately the same as before and after blockade, but in the total spinal anesthetized animals these pressures were ea. 30 mm Hg lower after blockade. Autonomic blockade. Autonomic blockade produces an apparent potentiation of epinephrine pressor response not by sensitization of the reacting structures, but by lowering the level of catecholamines available to the receptor sites and shifting the dose-response curve to the left.

Department of Pharmacology
Marquette University
School of Medicine
Milwaukee, Wisc.

2811 Schain, R. J. Some effects of a monoamine oxidase inhibitor upon changes produced by centrally administered amines. *British Journal Pharmacology & Chemotherapy* 1961, 17, 261-266.

In cats treated with s.c. or i.p. pheniperezine, the effects of 5HT injected into the lateral cerebral ventricle were greatly intensified and prolonged; the effects of epinephrine were potentiated to a lesser degree. Those of levartenenol, dopamine and tryptamine were not intensified and were prolonged to only a slight degree.

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2812 Lee Peng, C. H., & Walsh, E. O'F.

Effects of morphine on uptake of glucose and synthesis of glycogen in muscle or normal and chronically morphinized rats. *Nature*, 1962, 196, 171.

In the search for the site of addicting action in hormonal systems, the affects of morphine in vitro on glucose uptake and glycogen synthesis rates in excized diaphragms from normal and chronically morphinized rats were studied using the experimental procedures of Gemmill (1940), Verzáar & Wenner (1948) and others. In the absence of added morphine there is no significant difference between rates of glucose-uptake by tissue from normal and chronically morphinized rats, but the mean glycogen content of the diaphragms of morphinized subjects is somewhat higher than that of saline-injected controls. The effects of morphine on glycogenesis or glycogenolysis are secondary to direct effect on glucose uptake. Morphine does not influence the rates of oxygen consumption and has a negligible effect on lactate production in vitro by diaphragms from both normal and chronically morphinized rats.

Department of Biochemistry
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China

2813 Soaje-Echagüe, E., & Lim, Robert K. S. Anticonvulsant activity of some carbinylureas. *Journal of Pharmacology & Experimental Therapeutics*, 1962, 138, 224-248.

Three carbinylureas, MA-321 (1-methylcyclohexylurea), MA-337 (1-methylcyclopentylurea) and MA-367 (1-ethylcyclopentylurea) given orally have been found to have anticonvulsant properties in rats and dogs. They are comparable in potency to such anticonvulsants as trimethadione and diphenylhydantoin. All 3 also have sedative-hypnotic, antiemetic, but little or no hypotensive effects. MA-337 and MA-367 afford protection against both electroconvulsions and chemoconvulsions, resembling carbromal and phenobarbital in these respects. MA-337 is effective at a lower antielectroconvulsant dose than diphenylhydantoin, on both single and daily dosage, while MA-367 is effective at a lower antichemoconvulsant dose than trimethadione on single but

not on daily dosage. The antielectroconvulsant effect of MA-367 improves on daily dosage, equalizing that of MA-337. No tolerance or cumulation to the lethal effects of either MA-337 or MA-367 occurs on daily dosage. MA-321 is an antichemoconvulsant like trimethadione, which offers no protection against electroconvulsions. It has about the same activity as MA-367 and trimethadione, and its antichemoconvulsant effectiveness undergoes less change on daily dosage than that of MA-367. It does not induce tolerance or cumulation to lethal effects. All 3 compounds, given orally at 15 and 22% of the A-LD₅₀ daily for 6 months, produce no abnormality of the cellular elements of the blood, or any pathological change in the liver, spleen, kidney or alimentary tract.

Miles Laboratories, Inc.
Elkhart, Indiana

2814 Westermann, E. O., Maickel, R. P., & Brodie, B. B. On the mechanism of pituitary-adrenal stimulation by reserpine. *Journal of Pharmacology & Experimental Therapeutics*, 1962, 138, 207-218.

The hypersecretion of ACTH produced by reserpine, syrosingopine, Ro 4-1284 and other compounds that exert a reserpine-like syndrome, is elicited by doses of the drugs which block the storage of brain amines by 50% (unanesthetized male Sprague-Dawley rats). However, the discharge of ACTH is not related to the change in stored levarterenol since depletion of brain levarterenol stores by means of α -methyl-metatyrosine produces a degree of adrenocortical activation identical with that in control animals and closely related to blockade of 5HT storage. Since the central activity of reserpine is also related to the blockade of 5HT storage and not to that of levarterenol, it is possible that the hypersecretion of ACTH results from the action of reserpine on neuronal pathways that monitor the anterior pituitary.

Pharmakologische Institut
Universität Frankfurt-am-Main,
Frankfurt-am-Main, Germany

2815 Mirkin, Bernard L., & Cervoni, Peter.

The adrenergic nature of neurohumoral transmission in the cat nictitating membrane following treatment with reserpine. *Journal of Pharmacology & Experimental Therapeutics*, 1962, 138, 301-308.

The influence of reserpine on tension development in the nictitating membrane following sympathetic nerve stimulation and exogenous catecholamine administration was investigated in cats. Tension development in response to nerve stimulation was decreased from ca. 9.68 g in controls to ca. 1.90 g in reserpinized preparations, indicating a decreased output of mediator. The effect of autonomic blocking agents was analyzed with regard to elucidating a cholinergic component in the neurally induced response of the nictitating membrane. Phenotolamine was virtually ineffective in inhibiting neurally evoked contractions of the reserpinized membrane. This lack of potency contrasted sharply to its marked blocking effect in normal animals. Methylatropine exerted no significant blocking effect on responses to nerve stimulation or catecholamine in either control or reserpinized preparations. Atropine in the range of 100 μ g/kg depressed both neurally and catecholamine induced responses in a nonspecific manner. β -TM-10 and bretylium abolished neurally induced responses in reserpinized animals. Cholinergic mechanism is not apparently involved in sympathetic transmission at the nictitating membrane.

Department of Pharmacology
State University of New York Downstate
Medical Center
Brooklyn, N. Y.

2816 Walaszek, Edward J., & Chapman, John E. Bulbocapnine: an adrenergic and serotonin blocking agent. *Journal of Pharmacology & Experimental Therapeutics*, 1962, 138, 285-290.

Bulbocapnine was found to have an adrenergic blocking effect on cat and dog blood pressure. This antagonistic effect was also seen on the isolated rabbit ear and isolated rabbit jejunum but not on the carbachol-stimulated rat uterus. Bulbocapnine had no effect on responses to isoproterenol but potentiated the responses to vasopressin on dog and not on cat blood pressure. It is concluded that bulbocapnine is an

α -adrenergic blocking agent and has no effect on β -adrenergic receptors. A 5HT antagonism by bulbocapnine was demonstrated on cat and dog blood pressure, isolated rabbit ear, isolated rabbit jejunum, and isolated rat uterus. The possible role of these antagonistic effects in the mechanism of experimental catatonia is briefly discussed.

Department of Pharmacology
Kansas University Medical Center
Kansas City, Kansas

2817 Mackintosh, J. H. Effect of strain and group size on the response of mice to "Seconal" anaesthesia. *Nature* 1962, 194, 1304.

In inbred mice of the CE and CBA strains, 5 weeks of age, were kept in groups of 30-50 for 1 week to allow acclimatization and were set up in experimental groups of 1,2 and 8 per cage. The animals were anesthetized 3 days after setting up the experiment and again a week later. Secobarbital (Seconal) was used i.p. and the dose was graded for body-weight in order to give a mean anesthetic time of ca. 20 min. A mouse was assumed anesthetized if it failed to give a righting reflex when placed on its back. The variants of the F₁ hybrids is considerably less than that of the parental stocks and secondly the strains themselves are different in their response, the CBA strain being more variable than the CE strain. The CE x CBA hybrid is more variable than the reciprocal cross and shows, as does the maternal strain, a high variation in groups of 8 animals that have been together for ten days, indicating some maternal effect. Thirdly the 2-per cage group is less variable than are the solitary animals or groups of 8-per cage.

UFAW Research Unit
Department of Medical Biochemistry and
Pharmacology Medical School
Birmingham, 15, Great Britain

2818 Giarman, N. J., & Pepeu, G. Drug-induced changes in brain acetylcholine. *British J. Pharmacol.* 1962, 19, 226-234.

In adult male Wistar rats, drug-induced depression of the CNS was shown generally associated with an elevation in the level of total cerebral acetylcholine. This generalization held true for a wide variety of depressant drugs with one notable exception: the subacute administration of reserpine, with which there was an increase in cerebral acetylcholine after the 1st dose, but a return to normal levels after subsequent doses, despite continued depression of the animals. Reduction in the level of total acetylcholine in the brain followed the administration of certain convulsants (pentetrazole and diberal), but no change was seen after the administration of several mildly exciting agents. The notable exceptions to this generalization were atropine and scopolamine, which significantly lowered brain acetylcholine in doses producing mild excitation in only some of the animals and no gross manifestations in the rest.

Department of Pharmacology
Yale University School of Medicine
New Haven, Conn.

2819 Borison, H.L., Fishburn, B.R., Bhide, N.K. & McCarthy, L.E. Morphine-induced hyperglycemia in the cat. *Journal of Pharmacology & Experimental Therapeutics*, 1962, 138, 229-235.

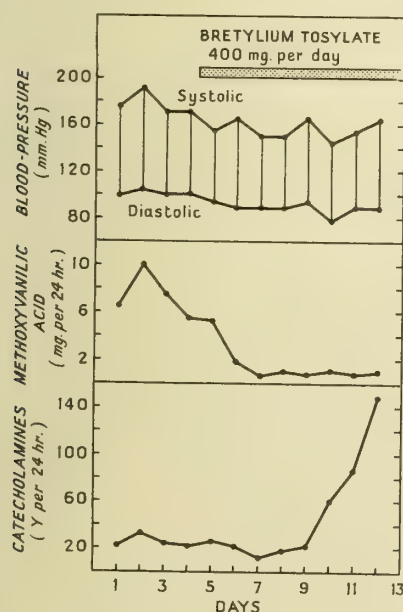
Intraventricular morphine evoked hyperglycemia of similar extent and time, but with only 1/25 to 1/50 of the dose requirement, as that elicited by i.v. administration of the drug. Morphine failed to elicit hyperglycemia after intracisternal injection. Morphine was at least as effective in eliciting hyperglycemia when injected intraventricularly in a small volume of solution, that localizes in the vicinity of the intraventricular foramen of Monro, as in larger volumes that distribute throughout the entire ventricular system. Intraventricular nalorphine, in a dose too small to be effective systemically, blocked the hyperglycemic effect of i.v. morphine. Intraventricular epinephrine was practically ineffective in evoking hyperglycemia. In contrast, lumbar intrathecal injection of epinephrine was even more effective than i.v. administration. Intrathecal epinephrine continued to evoke hyperglycemia after spinal cord ligation above the level of injection. Ablation of

area postrema did not alter hyperglycemic responses elicitable either with morphine or epinephrine. Morphine induces hyperglycemia reflexly by action on a paraventricular receptor site, probably located near the foramen of Monro. No central component in the hyperglycemic action of epinephrine is apparent.

Department of Pharmacology
University of Utah College of Medicine
Salt Lake City, Utah

2820 Le Moli, Salvatore, Pagliaro Luigi, & Mannino, Vincenzo. Urinary excretion of methoxy-vanilic acid and catecholamines in patients treated with bretylium tosylate. *Lancet*, 1962, No. 7263, 994-995.

Four patients given daily doses of 400-600 mg bretylium tosylate and were assayed for catecholamines, methoxyvanilic acid (urine) and blood pressure also 11 patients were followed for methoxyvanilic acid excretion. There was a definite dissociation between methoxyvanilic acid and catecholamine excretion as was shown in results from 1 patient given in the chart below.



Clinica Medica
Università di Palermo, Sicily

2821 Evans, W. C., & Stevenson, N.A. Studies of *Datura leichhardtii* Muell. ex

Benth. Part I. The anatomy of the leaf and stem. *Journal of Pharmacy & Pharmacology*, 1962, 14, 664-678.

Datura leichhardtii is readily distinguished from other species of the genus by its general morphology. Although similar to that of *D. stramonium*, the microscopy of the leaf differs in the length of the clothing trichomes and often in the form of the calcium oxalate crystals; it may be distinguished from other members of the Section Dutra, with the exception of *D. metel*, by the form and abundance of trichomes. *D. leichhardtii* differs from *D. metel* in possessing on the lamina of the leaf, glandular trichomes with uniseriate stalk and a single-celled head. The values of palisade ratio and stomatal index are within the same range as those of allied species.

University of Nottingham
Nottingham, Great Britain

2822 Mijan, Dominguez C. Estudio sobre la posibilidad de potenciación de los psicofarmacos por la procaina. [Study on the possibility of potentiating psychopharmaka with procaine.] *Archivos Instituto Farmacología Experimental*, 1962, 14, 91-129.

Imiprimine, hydroxyazide and chlorpromazine were studied in pentobarbital narcotized cats. Procaine (5-20 mg/kg) was used before treatment with the psychoactive drugs in order to ascertain possible potentiation. Imiprimine was potentiated by procaine, as was hydroxyzine, however chlorpromazine was not.

Instituto de Farmacología Experimental
Consejo Superior de Investigaciones Cientificas
Madrid, Spain

2823 Nichols, John R. Addiction-prone and addiction-resistant rats. *American psychologist*, 1962, 17, 398. [Abstract]

When subjected to a previously reported procedure, some rats develop sustained opiate-directed behavior (are addiction prone), but others do not (are addiction resistant). Would the offspring of addiction-prone crosses and those of addiction-re-

sistant crosses show behavior like that of their parents? The subjects, rats from previous experiments, were placed into ultra high, high, low, and ultra-low groups in terms of their morphine intake on relapse tests. The F_1 offspring of intra-group crosses were the experimental subjects. The offspring showed differences both in addiction proneness and in certain other variables.

[No address]

2824 Shimamoto, Takio, Ishioka, Tadao, & Fujita, Tsutomu. Antithrombotic effect of monamine oxidase inhibitor (Nialamide). Circulation Research, 1962, 10, 647-657.

Nialamide was compared with phenindione and warfarin for ability to prevent experimental thrombosis produced in rabbits. Rabbits were subjected to quantitative traumatization of the endothelial surface of the retroauricular artery and marginal ear vein. Pretreatment of the animals with 3-5 mg/kg nialamide, which did not prolong the 1 stage prothombin time (Quick), was much more effective in preventing thrombosis than either phenindione or warfarin, both of which prolonged the prothrombin time markedly. While 1.5 mg/kg nialamide was ineffective, concomitant application of subeffective doses of 150 mg phenindione and 1.5 mg nialamide was found effective. Nevertheless addition of larger amounts of phenindione did not enhance the antithrombotic effect of nialamide. Nialamide prevents the aggregation of platelets.

Department of Clinical Physiology and
Medicine
Tokyo Medical and Dental University,
Tokyo, Japan

See also 2574, 2587, 2594, 2649, 2851,
2852, 2853, 2854, 2859

2825 Chapman, Loring F., Walter, Richard D., Adey, W. Ross, Crandall, Paul H., Rand, Robert W., Brazier, Mary A. B., & Markham, Charles H. Altered electrical activity of human hippocampus and amygdala induced by LSD-25. *Physiologist*, 1962, 5, 118. [Abstract]

LSD (25-50 μ g) was administered by mouth to 5 subjects in whom bipolar electrodes had been stereotactically implanted bilaterally in the amygdala and in several hippocampal regions 2 weeks previously for evaluation in the surgical treatment of psychomotor epilepsy. With this amount of LSD only minimal subjective and behavioral changes were apparent, and no significant alteration in the scalp EEG could be discerned. However high amplitude slow waves and frequent bursts of paroxysmal spike discharges were observed from the depth sites beginning 25-30 minutes after ingestion and persisting for several hours. These alterations were maximal when environmental stimulation was at a low level and they could be greatly reduced by conversing with the patient or requiring him to perform simple tasks, e.g., serial subtraction.

University of California Medical Center
Los Angeles, Calif.

2826 Aprison, M. H., & Folkerth, T. L. Relationship between cerebellum and liver monoamine oxidase activity. *Physiologist*, 1962, 5, 100. [Abstract]

During the determination of MAO activity by the microdiffusion (NH_3) technique in the telencephalon, diencephalon plus optic lobes, medulla oblongata-pons, cerebellum and liver from normal Carneaux pigeons, the SD's of the means of the cerebellar and liver samples were found very large compared to those of other parts. Tyramine (10 mM) at 30°C, pH 7.2 was used as a substrate. A linear relationship existed between cerebellar and liver MAO activity with a coefficient correlation of 0.89. The same relationship was found in guinea pigs. In pigeons injected with different amounts of tranylcypromine or pheniprazine, the relationship between the organs held, however the slope of the curve was changed.

Apparently liver MAO activity changes more rapidly than that in the cerebellum. The liver-cerebellar type of correlation was not evident between the liver and other brain parts.

Institute of Psychiatric Research
Indiana University Medical Center
Indianapolis, Ind.

2827 Roa, P. Dante, Tews, J. K., & Stone, W. E. Anti-convulsive and neurochemical effects of amino-oxyacetic acid. *Physiologist*, 1962, 5, 204. [Abstract]

Aminooxyacetic acid (AOAA), which inhibits GABA conversion to succinic semialdehyde, was given i.v. to dogs for the recording of the cortical EEG activity and freezing of the brain in situ. A 20 mg/kg, AOAA has little effect on cortical activity while at higher doses there was some depression. Normally a dose of 20 mg/kg thiosemicarbazide or 15 mg/kg pentetrazol induced a severe seizure; a several-fold increase in the dose was required for this response after 20 mg/kg AOAA. Cerebral tissue was analyzed for 22 free amino acids and related substances by ion exchange chromatography, and for ammonia, glutamine and citrate. At various dosages AOAA induced large increases in brain GABA, ammonia, glutamine and tyrosine. Small increases in alanine and lysine and a decrease in aspartic acid. Convulsant doses of thiosemicarbazide alone induced a decrease in GABA and small increases in ammonia and alanine (observed during the seizure). With large doses of thiosemicarbazide after AOAA, the chemical pattern during the seizure was essentially the same as with AOAA alone. Hence the seizure cannot be attributed to low GABA or other observed chemical changes. Convulsant doses of pentetrazol alone induced small increases in ammonia; GABA did not decrease, and other constituents measured did not significantly change. With large doses of pentetrazol after AOAA, the chemical pattern during the seizure was like that with AOAA alone.

Department of Neurology and Physiology
University of Wisconsin
Madison, Wis.

2828 Cammarota, Hector E., & de Cammarota, Amalia C. La determinacion del acido 5-hidroxiindolacetico en orina. Su importancia en los casos de tumores carcinoides. (La serotonina y su metabolito.) [Determination of 5-hydroxyindolacetic acid in the urine. Its importance in cases of carcinoid tumors (serotonin and its metabolite)] Prensa Médica Argentina, 1962, 49, 671-674.

The method of McFarlane et al. and the method of Udenfriend et al. were used in the assay of 24-hour urine samples for 5HIAA (daily average by the 1st method 6.3 mg compared with 5.9 mg). Results of determinations from 28 patients suffering from carcinomata were given, and these tests advocated as of much use in this type of case as in the study of mental patients.

Laboratorio Bioquimico Servicio de Cardiología
Yerbal 2924
Buenos Aires, Argentina

2829 Ross, John J., Jr., Flanagan, Thomas L., & Maass, Alfred R. In vitro metabolism of 2-chloro-10-(3-dimethylaminopropyl)-phenothiazine. III. Isolation and identification of metabolites. Journal of Medicine and Pharmaceutical Chemistry. 1962, 5, 1035-1041.

The metabolism of chlorpromazine by rat and rabbit liver homogenates was studied chromatographically using isotope techniques. Three metabolites of the -(N-methyl)-C¹⁴ or S³⁵ labeled drug were isolated and identified as C¹⁴O₂, HO¹⁴HO and 2-chloro-10-(-3-methylaminopropyl)-phenothiazine-S³⁵. The effects of various inhibitors upon the oxidation of chlorpromazine-(N-methyl)-C¹⁴ in the rat liver homogenate system were also investigated.

Research and Development Division
Smith Kline & French Laboratories
Philadelphia 1, Pa.

2830 Axelrod, Julius. Enzymatic formation of morphine and nicotine in a mammal. Life Sciences, 1962, 2, 29-30.

Incubation of the soluble supernatant fraction of rabbit lung with 2-adenosylmethionine-methyl-C¹⁴ and normorphine resulted in a radioactive compound extractable with isoamyl alcohol at pH 9.5 which acted chromatographically as authentic morphine. After elution with water this compound was recrystallized and added to carrier morphine. The specific activity of morphine did not decrease after 3 recrystallizations. These observations were taken as evidence that an enzyme in rabbit lung can transfer the methyl group of S-adenosylmethionine to normorphine to form morphine. Similar experiments were run with the following nor compounds: norpethidine, norcodeine and nornicotine. In all cases compounds were obtained with the chromatographic properties of, respectively, pethidine, codeine and nicotine.

NIMH
Bethesda, Md.

2831 Cession-Fossion, A., & Michaux, R. Activités pharmacodynamiques comparées de la 5-hydroxytryptamine et de la 5-methoxytryptamine. [The comparison of the pharmacodynamic activities of 5-hydroxytryptamine and 5-methoxytryptamine.] Life Sciences, 1962, 2, 483-486.

Carotid blood pressure was registered with a manometer in anesthetized tracheotomized rats. Injections were made into the jugular vein. Cat nictitating membrane, after preganglionic stimulation of the cervical sympathetic nerve, was also used in assay. Guinea pig ileum was also used as an assay as a test material. Methylation of 5HT to 5 methoxytryptamine (5MT) changes little of its action on blood pressure in the rat and cat, and its contractile action on isolated ileum. Methylation slightly increases the potentiating action of 5HT on the presynaptic orthosympathetic stimulation of the nictitating membrane. Previous large doses of 5MT (to a total of 180 µg/kg) do not influence the response of rat blood pressure to 5HT. Some inhibitors of 5HT action have a similar effect on 5MT response but at lower dosage levels.

Institut Léon Fredericq
Physiologie et Biochimie
Université de Liège
Liège, Belgium

2832 Boggs, Dallas E., & Waisman, Harry A. Effects on the offspring of female rats fed phenylalanine. *Life Sciences*, 1962, 2, 373-376.

Female Holtzman rats were fed either 5 or 7% L-phenylalanine, or 4% DL plus 3% L-phenylalanine added to a commercial diet throughout pregnancy and lactation. At 1 - 6 days of age the young were bled and tyrosine and phenylalanine levels of pooled plasma determined. For controls phenylalanine and tyrosine levels were respectively 2.6 and 3.7 mg/100 ml. For the 5% level comparable results were 2.9 and 2.7 while for the 7% level these were 4.3 and 2.1. For 4% DL + 3% L comparable results were 6.8 and 5.5. The addition of the DL mixture 2 dams receiving the L form causes a greater increase in blood levels in the sucklings than if L-phenylalanine is fed alone.

Department of Pediatrics
University of Wisconsin
Madison, Wisc.

2833 Costa, E., Kuntzman, R., Gessa, G. L., & Brodie, B. B. Structural requirements for bretylium and guanethidine-like activity in a series of guanidine derivatives. *Life Sciences*, 1962, 2, 75-80.

Seven guanidine derivatives were assayed for activity in Sprague-Dawley rats by the reduction of heart levarterenol 7 hours after administration of 7.5 mg/kg of the drug i.v. Bretyliumlike activity was measured by the ability of various doses of these drugs to prevent loss in heart levarterenol induced by 5 mg/kg guanethidine i.v. Heart levarterenol was assayed spectrofluorimetrically (Shore and Oline 1958). Administration of guanethidine induced levarterenol depletion was 49% of normal with bretylium and ran from 0 to 86% with the guanethidine derivatives. These agents brought transmission at peripheral and adrenergic nerve terminals without antagonizing catecholamines when given. Compounds such as bretylium prevent the normal release of levarterenol as well as that induced by guanethidine, while others such as guanethidine deplete levarterenol perhaps by persistent stimulation of the process normally activated by nerve impulses. Compounds

having a strong basic group (guanidine or a quaternary ammonium) separated from a benzene ring by 1 carbon atom appear to exert bretyliumlike effect; in contrast a strongly basic nitrogen separated from a ring by 2 carbons appears to elicit a guanethidinelike effect.

Laboratory of Chemical Pharmacology
National Heart Institute
Bethesda 14, Md.

2834 Desaty, D., O. Hadzija, S. Iskrić, D. Keglević, & S. Kveder. The synthesis of N-acetylserotonin. *Biochimica Biophysica Acta*, 1962, 62, 179-180.

Starting with 5-benzyloxytryptamine HCl, N-acetylserotonin was synthesized and identified using paper chromatography.

Tracer Laboratory
Institute "Ruder Boskovic"
Zagreb, Yugoslavia

2835 Robinson, Robert L., & Watts, Daniel T. Inhibition of adrenal secretion of epinephrine during infusion of catecholamines. *American Journal of Physiology*, 1962, 203, 713-716.

The effect of i.v. infusion of epinephrine or levartenenol on the secretion of epinephrine by the adrenal gland was studied in dogs. The epinephrine content of adrenal venous blood was assayed on the rat uterus, automatically stimulated. The infusion of epinephrine or levartenenol at a rate which produced an increase in blood pressure inhibited the output of epinephrine by the adrenal. If the rate of infusion of catecholamines was too slow to increase the blood pressure, or if the increase in blood pressure was prevented by a pressure compensator, secretion of epinephrine was not inhibited. A good correlation exists between the percent decrease in epinephrine secretion and the percent increase in blood pressure produced by infusion of catecholamines. The inhibition of epinephrine secretion during infusion of catecholamines is produced reflexly by the induced increase in blood pressure. In two experiments the aortic epinephrine concentration exceeded the adrenal venous epinephrine concentration

during infusion of epinephrine, suggesting an uptake of epinephrine by the adrenal gland.

Department of Pharmacology
West Virginia University Medical Center
Morgantown, West Va.

2836 Brune, Guenter G., & Himwich, Harold E. Indole metabolites in schizophrenic patients. *Archives of General Psychiatry*, 1962, 62, 324-327.

Longitudinal studies of the urinary excretions of tryptamine and total indole-3-acetic acid as well as of behavior were made on 20 male schizophrenic patients. The average urinary output of tryptamine did not differ from normal values when all data were considered. There was only a slight elevation of total indole-3-acetic acid when compared with results obtained on normal subjects. For both indole derivatives, however, a wide range of variation was noted in individual patients. A striking correlation between excretion of tryptamine and total indole-3-acetic acid with the degree of psychotic activity was noted, both indoles attained increasingly high abnormal levels with increase in the severity of the psychosis. Also there was a reduction of indoles toward or to normal levels occurring with improvement in the mental state. Each of the 2 different biochemical patterns, 1 occurring with activation of the psychotic symptoms and the other with a reduction, retained its distinctive features whether or not reserpine was administered.

Thudichum Psychiatric Research
Laboratory
Galesburg State Research Hospital
Galesburg, Ill.

2837 Fessel, W.J. Autoimmunity and mental illness. *Archives of General Psychiatry*, 1962, 62, 320-323.

Sera was subjected to the brain-latex test, the kidney-latex test, FII agglutination tests and analytical ultracentrifuge. Sera from 85 normal blood donors was obtained, and sera taken from 72 patients with acute mental disturbances within 24 hours of their admission. As well samples were

obtained from 185 chronically psychotic patients from a state mental hospital; 28% of the acutely disturbed mentally ill patients had a serum substance, primarily protein, which reacted with a brain constituent. The incidence of such serum substances in chronically psychotic patients was 15%, in general hospital patients 11% and in blood donors 10%.

Langley Porter Neuropsychiatric Institute,
San Francisco, Calif.

2838 Marks, B.H., Samorajski, T., & Webster, E.J. Radioautographic localization of norepinephrine- H^3 in the tissues of mice. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 376-381.

The radioautographic localization of levarterenol- H^3 in some tissues of mice has been described. In the 1st few minutes after injection, binding to storage sites was not prominent, but for some hours afterward, specific localization in sharply defined regions of tissues was noted. In the heart, long thin fibers, lying alongside myocardial cells, showed very intense labeling. In the spleen, short fibers in trabeculae and small "buttons" in splenic pulp appeared to be storage sites. In the small intestine, marked uptake of levarterenol was observed in polymorphic masses scattered throughout the regions of Auerbach's plexus, including those areas which could be demarcated as ganglia in this layer. In the kidney, storage of levarterenol was occasionally observed in fibers at the vascular pole of some glomeruli. In the adrenal, the medulla became heavily labeled, while the cortex demonstrated no storage of levarterenol. The sites of levarterenol storage in the tissues described were nerve endings of the sympathetic postganglionic system.

Ohio State University College of Medicine
Cleveland, Ohio

2839 Iversen, L.L., & Whitby, L.G. Retention of injected catechol amines by the mouse. *British Journal of Pharmacology*, 1962, 19, 355-364.

The importance of tissue storage as a method of inactivation of circulating catecholamines has been assessed by measuring the amount of unchanged hormone remaining in the mouse 30 minutes after the injection of various doses of H^3 -epinephrine or H^3 levarterenol. This method of inactivation is quantitatively more important for levarterenol than for epinephrine at all dosage levels studied. For both hormones, storage is relatively more important at physiological dose levels (3 - 30 $\mu g/kg$) than at higher dose levels (150-300 $\mu g/kg$). The results obtained after the simultaneous injection of various doses of H^3 -epinephrine and C^{14} levarterenol show that circulating epinephrine and levarterenol compete for entry into these sites, a view put forth by Strömbblad & Nickerson (1961).

Department of Biochemistry
University of Cambridge
Cambridge, Great Britain

2840 Belford, Julius, & Feinleib, Marcia R. The increase in glucose-6-phosphate content of the heart after the administration of inotropic catecholamines, calcium, and aminophylline. *Biochemical Pharmacology*, 1962, 11, 987-994.

Content of glucose-6-phosphate in heart was determined after the treatment of intact cats with cardiotonic agents. Epinephrine, levarterenol and isoproterenol significantly increase the amount of the catecholamines, i.e., isoproterenol 8 epinephrine = levarterenol. Controlled rate experiments indicate that increases in glucose-6-phosphate produced by epinephrine are related to increased force of contraction. Present studies on the isolated and intact rat heart further support these observations pertaining to epinephrine. In the intact cat, calcium and aminophylline also produce significant elevations in the content of glucose-6-phosphate in the right and left ventricles and left auricle concomitant with their cardiotonic action.

Department of Pharmacology
State University of New York
Downstate Medical Center
Brooklyn, N.Y.

2841 Atkinson, R., & Wynne, N.A. A method for the estimation of adrenaline and noradrenaline in urine. *Journal of Pharmacy and Pharmacology*, 1962, 14, 794-797.

A method for the estimation of epinephrine (adrenaline) and levarterenol (noradrenaline) in urine is described. The catecholamines are absorbed on aluminum oxide and eluted with acid. The epinephrine and levarterenol are estimated separately after oxidation with manganese dioxide at different pH values and converted to the trihydroxyindole derivative for fluorimetric estimation. A mean recover of 82% ($\pm 5\%$ S.D.) was obtained for total amines estimated as epinephrine, which recovery was 83% ($\pm 6\%$ S.D.), while levarterenol recovery was 80% ($\pm 6\%$ S.D.). The results were in good agreement with biological assay results.

Department of Pharmacy
Sunderland Technical College
Newcastle-on-Tyne
Great Britain

2842 Udenfriend, Sidney, Zaltzman-Nirenberg, Perola. On the mechanism of the norepinephrine release produced by α -methyl-meta-tyrosine. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 194-199.

It has been shown that α -methyl-meta-tyrosine (α MMT) must be decarboxylated in order to bring about release of levarterenol (norepinephrine) from tissues. α -Methyl-meta-tyramine and aramine, metabolic products of α MMT, are even more potent with respect to levarterenol releasing activity. Thus α MMT, and no doubt α -methyldopa, represent unique ways of administering the corresponding pharmacologically active amines. Far less than stoichiometric amounts of the α -methyl-meta tyramines are required to bring about and maintain depletion of levarterenol (compounds injected i.p. into guinea pigs).

Laboratory of Clinical Biochemistry
National Heart Institute
NIH
Bethesda, Md.

2844 Burack, W.R., & Draskóczy, P.R. The mode of secretion of catecholamines from the adrenal medulla. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 165-169.

The possibility that the heavy storage granules represent the sole immediate source of the catecholamines which are secreted by the adrenal medulla was tested in vivo. Rats were treated with tritiated DOPA of high specific activity so that labeled catecholamines were made and stored in the adrenal glands. The specific activity of the stored hormones was found to be the same as the specific activity of the hormones secreted into the adrenal vein. This finding supports the proposal that a degranulation mechanism operates and viates the proposition that a small but dynamic extragranular pool shunts freshly formed catecholamines past the granules directly into the blood. In the rat anesthetized with pentobarbital and subjected to laparotomy, the biological half-life of the catecholamines in the adrenal gland is 1 day, while others have found that under experimental conditions which involved no anesthesia or surgery, the life-life is 10 days.

Department of Pharmacology
Harvard Medical School
Boston, Mass.

2844 Moore, K.E., & Gosselin, R.E. Effects of 5-hydroxytryptamine on the anaerobic metabolism and phosphorylase activity of lamellibranch gill. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 145-152.

The effects of 5HT and certain other cilioactive agents were studied on the anaerobic metabolism of excised gills of the clam, *Modiolus demissus*. In these gills endogenous glycogen serves as a substrate and lactic acid is a product of anaerobic glycolysis. The rate of anaerobic glycolysis but not of glucose uptake is markedly stimulated by low concentrations of 5HT. At relatively high concentrations 5HTP and epinephrine stimulate while acetylcholine inhibits the rate of anaerobic lactic acid production. BOL blocks but LSD mimics the

5HT effects. The actions of 5HT on the carbohydrate metabolism of these gills cannot be ascribed to an activation of gill phosphorylase.

Department of Pharmacology and
Toxicology
Dartmouth Medical School
Hanover, New Hamp.

2845 Alexander, George J., & Alexander, Rita B. Effect of Metrazol on isolated mammalian cells. II. Inhibition of synthesis of cholesterol. *Biochemistry*, 1962, 1, 783-788.

Mouse L cells grown in medium containing 4×10^{-6} M pentetrazol (Metrazol) had a lower sterol content than control cultures. Cells incubated in the presence of the drug with acetate- 1-C^{14} incorporated 1/3 of the radioactivity normally incorporated. Cells grown in the presence of pentetrazol but incubated in drug-free media rapidly synthesized sterols of high specific activity. Rigorous analysis of the sterol fraction indicated that 79% of the radioactivity was present in cholesterol.

Department of Biochemistry
New York Psychiatric Institute
New York, N.Y.

2846 Eberhardt, H., Freundt, K.J., & Langbein, J.W. Der dünn-schicht-chromatographische Nachweis von Schlafmitteln als Reinsubstanzen und nach Körperpassage. [Thin-layer chromatography of hypnotic drugs as pure compounds and after passage through the body.] *Arzneimittel-Forschung*, 1962, 12, 1087-1089.

Twelve sedatives and hypnotic drugs, mostly barbiturates, were extracted from human urine (45 ml) with ether, washed, purified and dried. Chromatography was carried out with "Kieselgel C" (Merck-Germany), after addition of eosin (1:1000). Piperidine-petroleum ether (1:5) was used as solvent, Hg-I-NO₃ as a developer and UV light for direct inspection. R_f values and data for identification of the pure drugs and their metabolites are presented. The density of spots allows estimation of urinary excre-

tion. The limit of detection varies according to drug between 5-10 μ g. The procedure can be carried out in 2½ hours.

Institut für Toxikologie der
Universität Tübingen
Tübingen, Germany

2847 Antoniades, G.I., Gillert, K.E., & Rudolph, E. Über den Ausfall von Luesreaktionen nach Vergiftungen durch Barbitursäurederivate. [The outcome of lues reactions after barbiturate poisoning.] *Zeitschrift für Haut- und Geschlechtskrankheiten*, 1962, 32, 81-86.

The "cardiolipin" microfluoroculation test was carried out in a sera of 48 patients with known barbiturate poisoning. There were no positive results.

Robert Koch-Institut
Berlin, Germany

2848 Fuchs, Anna-Rita, & Fuchs, Fritz. Urinary excretion of 5-hydroxyindoleacetic acid during the menstrual cycle. *Danish Medical Bulletin*, 1962, 9, 39-45.

Urinary excretion of 5HIAA during the menstrual cycle was studied in 2 women, with morning urine samples. Udenfriend's assay procedure was used and the influence of food and alcohol were studied. Characteristic cycle variations were reported, an increased in average excretion rate during the luteal rather than the follicular phase. Ovulation was accompanied by a peak in 5HIAA excretion, while a drop was observed at the onset of menstruation. A possible correlation may exist between the rate of 5HIAA excretion and the number of circulating platelets.

Department of Medical Physiology
University of Copenhagen
Kommunchospitalet, Copenhagen
Denmark

2849 Lafferty, John J., Garvey, Eleanor, Nodiff, Edward A., Thompson, Walter E., & Zirkle, Charles L. The synthesis of phenothiazines. VII. Methyl- and arylsul-

fonylation of phenothiazine and its 10-substituted derivatives. *Journal of Organic Chemistry*, 1962, 22, 1346-1351.

3-Methyl-, 3-phenyl-, and 3-p-tolylsulfonylphenothiazine were obtained from the reactions of phenothiazine or its 10-sulfonyl derivatives with the corresponding sulfonyl chlorides in the presence of aluminum chloride. The same products also were obtained from the rearrangement of the corresponding 10-sulfonyl derivatives in the presence of aluminum chloride. 3-Methylsulfonylphenothiazine also was prepared by a Smiles rearrangement of 2'-formamido -2-nitro -4-methylsulfonyldiphenyl sulfide.

Smith Kline and French Laboratories
Philadelphia, Pa.

2850 Sicuteri, F., Franchi, G., Michelacci, S., & Salmon, S. Aumento della escrezione urinaria dell'acido vanilmandelico - catabolita delle catecholamine - durante l'accesso emicranico. [Increase in the urinary excretion of vanilmandelic acid - catabolite of catecholamines - during migraine attacks.] *Settimana Medica*, 1962, 50, 13-16.

Ten patients, 6 women and 4 men, aged 34-56 years, were studied in relation to vanilmandelic acid excretion. No drugs were administered and coffee and chocolate prohibited. During attacks vanilmandelic acid excretion was elevated to as high as 12 mg/24 hours, and levels subsided to normal on recovery.

Clinica Medica dell'Università di Firenze
Florence, Italy

2851 Winthrop, Stanley O., Davis, M.A., Myers, G.S., Gavin, J.G., Thomas, R., & Barber, R. New psychotropic agents. Derivatives of dibenzo [a,d]-1,4-cycloheptadiene. *Journal of Organic Chemistry*, 1962, 27, 230-240.

A series of 5-dialkylaminoalkyl-5-hydroxydibenzo [a,d]-1,4-cycloheptadienes was prepared by alkylating dibenzo [a,d]-1,4-cycloheptadien-5-ones with basically sub-

stituted Grignard reagents. The corresponding 5-dialkylaminoalkyl- and 5-dialkylidenedibenzo [a,d]-1,4-cycloheptadienes were also synthesized. Other alkylation procedures were adopted in instances where the Grignard method was unsuitable. Many of the compounds possess pharmacological activities characteristic of psychotropic agents. Some of the relationships between structure and activity are briefly mentioned. In general these compounds exhibited a spectrum of pharmacological activities characteristic of both tranquilizers and antidepressants. They reduced spontaneous motility, potentiated narcosis, caused hypothermia and were anticonvulsants.

Ayerst Research Laboratories
Montreal, Quebec
Canada

2852 Saito, Seiichi, & May, Everette, L. Structures related to morphine. XXI. An alternative synthesis of diastereoisomeric 2'-hydroxy-2,5,9-trimethyl-6,7-benzomorphans. *Journal of Organic Chemistry*, 1962, 27, 1087-1089.

Cyclization of 2-(p-methoxybenzyl)-1,3,4-trimethyl-1,2,5,6-tetrahydropyridine with 48% hydrobromic acid leads to a mixture of diastereoisomeric benzomorphans IV and VI in a ratio of about 12:1, respectively (May and Ager 1959). The analgesic activity in mice of the lesser isomer (VI) was 7 times that of IV and 5 times that of morphine. Efforts to increase the yield of VI in the above mentioned ring closure have been unsuccessful and therefore attention was settled on the 9-methylcarbonyl (I; May and Kugita), the methoxy relative of which had previously been converted to 2,5,9-trimethyl-6,7-benzomorphans (May and Fry 1957) by catalytic hydrogenation of the corresponding 9-methylene derivative. By a similar sequence of reactions either IV or VI can be obtained depending on the medium used in the hydrogenation of the 9-methylene compound (II).

National Institute of Arthritis and
Metabolic Diseases
NIH
Bethesda 14, Md.

2853 Saito, Seiichi, & May, Everette L. Structures related to morphine. XX. Stevens reaction in the synthesis of 5-ethyl-2'-hydroxy-2-methyl-(or phenethyl)-6,7-benzomorphans. *Journal of Organic Chemistry*, 1962, 27, 948-951.

The Stevens reaction was applied to the synthesis of 5-ethyl-2'-hydroxy-2-methyl (and -phenethyl)-6,7-benzomorphans (V). The 2-methyl compound (Va) was converted to the 2-phenethyl analog (Vb) and to 1-ethyl-7-methoxynaphthalene by standard reactions. Va has no morphinelike properties at 2 and 4 mg/kg in addicted monkeys stabilized on 3 mg/kg at morphine. The N-phenethyl analogue Vb, likewise does not suppress morphine abstinence at 0.5 and 1.0 mg/kg, gives only slight suppression at 2-8 mg/kg but appears to have complete morphinelike physical dependence capacity with strong stimulant action at 15 mg/kg. Thus Vb is rated intermediate in physical dependence properties. However it is evident that this ratio of its analgesic dose (0.16 mg/kg) in mice to the stabilizing dose (16 mg/kg) in monkeys is nearly 100 times more favorable than that of morphine (2 mg/kg to 3 mg/kg).

National Institute of Arthritis and
Metabolic Diseases
NIH
Bethesda 14, Md.

2854 Kadin, Saul B., & Cannon, Joseph G. Esters of N-methyl-3-hydroxy-piperidine having psychotomimetic activity. II. *Journal of Organic Chemistry*, 1962, 27, 240-245.

A series of esters of N-methyl-3-hydroxy-piperidine were prepared by transesterification of their corresponding methylesters (except for N-methyl-3-piperidyl fluorene-9-carboxylate for which the ethyl ester was used). The esters containing the cyclopropyl and the cyclobutyl groups exhibited marked psychotic activity. In general, the 9-substituted fluorine-containing esters were more active than their corresponding unsubstituted diphenylmethane analogues. Also those compounds exhibiting maximal psychotomimetic activity contained a hydroxyl group alpha to the carboxyl moiety.

Division of Pharmaceutical Chemistry
School of Pharmacy
University of Wisconsin
Madison 6, Wisc.

2855 Shapiro, Seymour L., Bandurco, Victor, & Freedman, Louis. Pyridylethylbarbituric acids. *Journal of Organic Chemistry*, 1962, 27, 174-178.

A series of 35 5-piperidylethylated barbituric acids was synthesized and the UV absorption spectra and pK_a noted.

U.S. Vitamin & Pharmaceutical Corporation
Organic Research Laboratories
Yonkers, N.Y.

2856 Mannino, V., & Pagliaro, L. Osservazioni su un metodo di dosaggio semiquantitativo dell'acido 3-metossi-4-idrossimandelico. [Observations on a semiquantitative assay for 3-methoxy-4-hydroxymandelic acid.] *Progresso Medico*, 1962, 118, 106-107.

The method of Gitlow et al. (1960) was modified for the determination of urinary catecholamines (ca. 80 % methoxymandelic acid) and the fluorometric assay method of Euler modified by Giotti and Ingianna (1959) was combined. The method was used largely in the detection of essential hypertension (total of 15 patients) and comparative results obtained from 26 normal subjects, and 16 other patients.

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Therapia Medica
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Palermo, Italy

2857 Javier Solduga Camarero, Francisco. Nueva técnica colorimétrica para la determinación de la 5-hidroxitriptamina [New colorimetric technique for determination of 5-hydroxytryptamine.] *Medicamenta*, 1962, 14, 70-71.

5HT was measured at 450 m μ in acetic-sulfuric acid solution using a Beckman model C photometer (intense violet color). The chromophore obtained has a maximal absorption at 275 m μ .

Instituto Español de Fisiología y Bioquímica
Barcelona, Spain

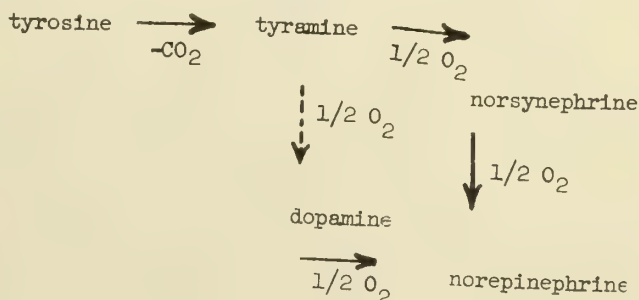
2858 Costa, E., Gessa, G.L., Kuntzman, R., & Brodie, B.B. A differential action of reserpine on brain dopamine stores in rabbit. *Life Sciences*, 1962, 2, 599-604.

After the injection of 2 mg/kg with reserpine to New Zealand White adult rabbits, 5HT stores in the brainstem were depleted for a period of 24-36 hours, and then rose slowly so that at 80 hours there was a 50% return of normal. Changes in brainstem levarterenol closely paralleled those of 5HT. After 0.5 mg/kg reserpine i.v. at 90 minutes, the depletion of dopamine stores in the carbate nucleus was almost complete in all subjects. In contrast 5HT depletion was variable, ranging from 40-80% of normal. Large doses of reserpine deplete the stores of all 3 amines, but dopamine remains depleted long after the central action of reserpine is terminated and the ability of the brain to store 5HT and levarterenol is partially restored. Threshold doses completely deplete dopamine stores, but lower 5HT stores to a variable degree. Central effects are not related to the dopamine levels.

Laboratory of Chemical Pharmacology
NIH
Bethesda, Md.

2859 Creveling, Cyrus R., Levitt, Morton, & Udenfried, Sidney. An alternative route for biosynthesis of norepinephrine. *Life Science*, 1962, 2, 523-526.

Studies with tyramine-2- C^{14} and norsyneprhine-3- H^3 were carried out in order to investigate the occurrence of the following metabolic conversions:



Biochemistry

Male rats were injected with the MAO inhibitor iproniazid, 150 mg/kg i.p. at 48-hour intervals. Twenty-four hours after the 1st dose of iproniazid, radioactive amine was administered and the conversion of tyramine and norsynephrine to levarterenol (norepinephrine) and nonmetanephrine, establishing the route diagramed above.

National Heart Institute
Bethesda, Md.

See also 2588, 2609, 2621, 2622, 2645,
2677, 2785

ABBREVIATIONS

-KG	α -ketoglutarate	GABOB	γ -amino- β -hydroxybutyric acid
ACL	Zuckerman's Affect Adjective Check List	HD	hypnotic dose
ACTH	adrenocorticotrophic hormone	5HIAA	5-hydroxyindoleacetic acid
ad lib.	free choice	5HT	5-hydroxytryptamine
ADP	adenosinediphosphate	5HTP	5-hydroxytryptophane
a.m.	morning		
AMA	American Medical Association	i.a.	intraarterial
Art.	Article	ibid.	in the same place
ATP	adenosinetriphosphate	i.e.	that is
		i.m.	intramuscular
BAL	British antiLewisite	IMPS	Lorr's Inpatient Multidimensional Psychiatric Scale
BAS	benzyl analogue of serotonin	i.p.	intraperitoneal
b.i.d.	twice a day	IPAT	Cattell's Institute for Personality & Ability Testing Anxiety Scale
BOL	bromolysergic acid diethylamide	I.Q.	intelligence quotient
BUN	blood urea nitrogen	IU	international unit
		i.v.	intravenous
C	Celsius scale		
a.	about	kg	kilogram
CAR	conditioned avoidance response	K _i	Michaelis constant for an inhibitor
CBS	chronic brain syndrome	K _m	Michaelis constant for a substrate
c	cubic centimeter		
CD	convulsive dose	lbs	pounds
m	centimeter	LD	lethal dose
m ²	square centimeter	LSD	lysergide
m ³	cubic centimeter		
C.N.R.S.	Centre National de la Recherche Scientifique	μ	micron
CNS	central nervous system	μ c	microcurie
COMT	catechol-o-methyl transferase	μ g	microgram
cps	counts per second	μ l	microliter
CR	conditioned reflex (response)	μ M	micromolar
CS	conditioned stimulus	m μ	millimicrons
CTD	Climbing Time Delay	M	molar
		ma.	milliamperes
DDT	dichlorodiphenyl trichloroethane	MACC	Motility Affect Cooperation Communication
DOPA	3, 4-dihydroxy-phenylalanine	MAO	monoamine oxidase
DPH	diphosphopyridine nucleotide	MAS	Taylor Manifest Anxiety Scale
DPNH	reduced diphosphopyridine- nucleotide	meq	milliequivalents
		ml	milliliter
ECG	electrocardiogram	mm	millimeter
Ed.	editor	mm ²	square millimeter
ED	effective dose	MMPI	Minnesota Multiphasic Person- ality Inventory
EDTA	ethylenediaminetetraacetic acid	MSRP	Multidimensional Scale for Rating Psychiatric Patients
EEG	electroencephalogram		
e.g.	for example	N	normal
ERG	electroretinogram	NEFA	nonesterified fatty acid
et al.	and others	NIMH	National Institute of Mental Health
etc.	and so forth		
F	Fahrenheit scale	p	probability
FFA	free fatty acid	PAH	para-aminohippuric acid
g	gram		
GABA	γ -aminobutyric acid		

PBI	protein-bound iodine	SRA	Science Research Associates
pH	negative logarithm of the hydrogen ion concentration	Suppl.	supplement
P _i	inorganic phosphate	TAT	Thematic Apperception Test
P.M.	afternoon and evening	TH	thyroid hormone
p.o.	by mouth	t.i.d.	thrice a day
ppm	parts per million	TPN	triphosphopyridinenucleotide
PRP	Psychotic Reaction Profile	TPNH	reduced triphosphopyridine-nucleotide
q.i.d.	four times a day	TSH	thyroid-stimulating hormone
refs.	references	U	unit
R _f	ratio of the distance of dissolved substance to solvent distance	UR	unconditioned response
RNA	ribonucleic acid	US	unconditioned stimulus
ru	rat unit	USAF	United States Air Force
s.c.	subcutaneous	USDHEW	United States Department of Health, Education, and Welfare
S.D.	standard deviation	USP	United States Pharmacopoeia
SGOT	serum glutamic oxaloacetic transaminase	USPHS	United States Public Health Service
SGPT	serum glutamic pyruvic transaminase	UV	ultraviolet
sic	exactly as found	VA	Veterans Administration
SOSAI	Springfield Outpatient Symptom and Adjustment Index	viz.	namely
		WAIS	Wechsler Adult Intelligence Scale
		WPRS	Wechsler Psychiatric Rating Scale

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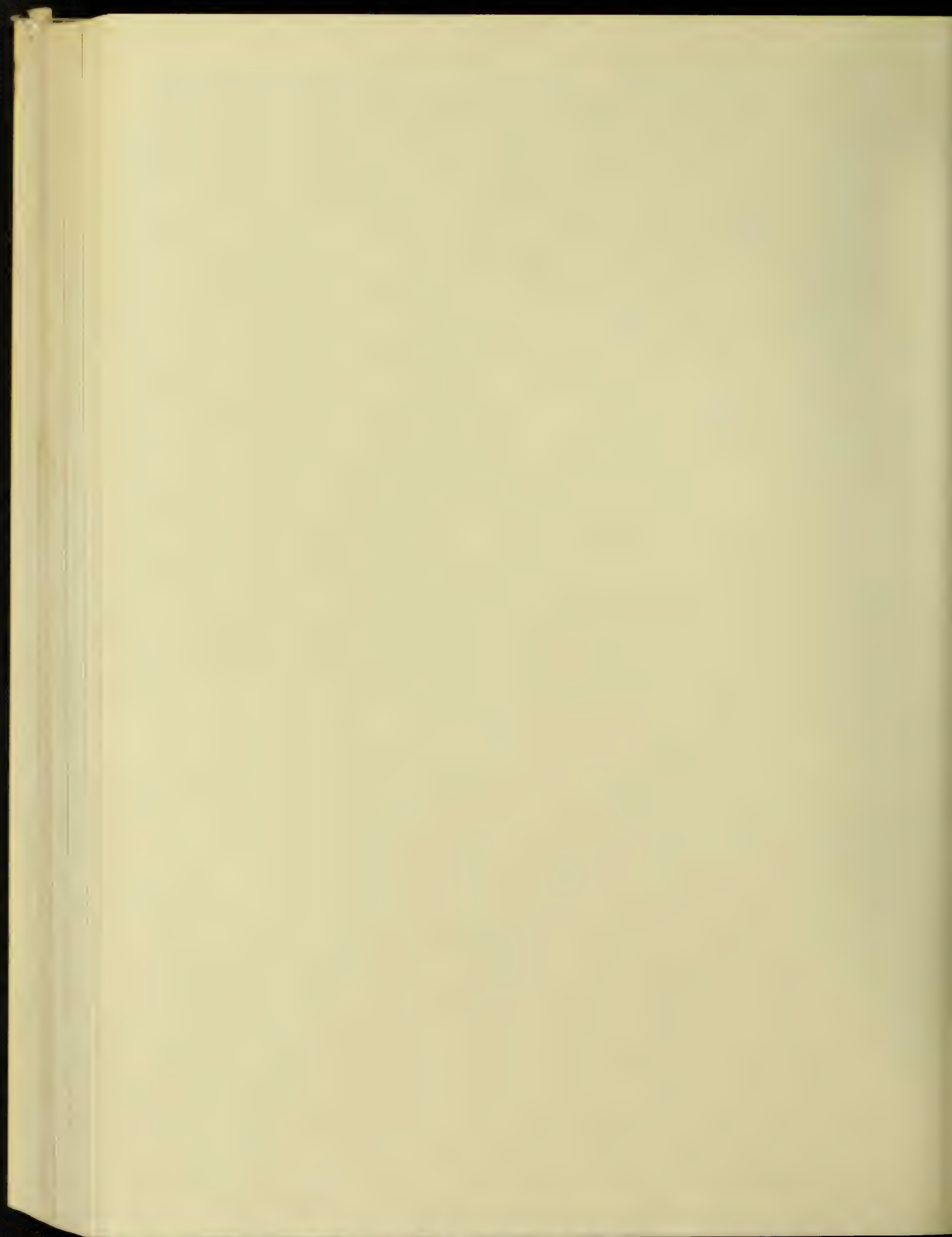
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Psychopharmacology ABSTRACTS

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PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results.

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PSYCHOPHARMACOLOGY ABSTRACTS

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REVIEWS, SUMMARIES, BIBLIOGRAPHIES,
AND GENERAL ARTICLES AND BOOKS

2860 Parkes, M. W. Tranquillizers In: Ellis, G.P., & West, G.B. [Eds.] Progress in Medicinal Chemistry. Volume 1. London: Butterworth & Co., Ltd., 1961. Pp. 72-131.

Phenothiazine, diphenylmethane and propanediol derivatives, and the Rauwolfia alkaloids are discussed at length in relation to history, pharmacological properties and clinical usage. Pharmacological tests applied to tranquilizers include those for: a) taming (a reduction of natural aggressiveness, timidity or anxiety); b) reduction of the responses of animals rendered active by operation--sham rage, septal animals; c) suppression of behavioral arousal response to noise (startle) or to electrical stimulation of the reticular formation or hypothalamus; d) suppression of EEG arousal response to sensory stimulation, electrical stimulation or injection of drugs (epinephrine, etc.); e) suppression of responsiveness of animals sensitized by solitary confinement or treatment with LSD, mescaline or harmine; f) suppression of CR's, including CAR's, classical and free-operant (Sidman), conditioned emotional response, free-operant reward performance and conditioned emotional disturbance of this, free-operant discrimination and conflict behavior; g) reduction of the hormonal effects of stress including adrenal ascorbic acid depletion, 17-ketosteroid excretion and various endocrine effects; h) reduction of spontaneous locomotor activity; i) reduction of body temperature of small animals; j) potentiation of depressant drugs, hypnotics and analgesics; k) antagonism to stimulant drugs including toxicity (amphetamine, mescaline), increased locomotor activity (amphetamine, caffeine, etc.), excitement (morphine, LSD, mescaline); l) impairment of muscular coordination including performance on inclined plane, rotarod or ladder, ataxia, catatonia; m) unconditioned avoidance of noxious stimulus (electric shock); n) reduction of reflex responses (pinna reflex, corneal reflex, paralysis, narcosis; p) anti-convulsant action, suppression of convulsions due to noise (audiogenic), electric shock or drugs (pentetrazol, nicotine, strychnine, etc.); q) antiemetic action, suppression of apomorphine emesis in dogs, and r) analgesic action, delay in response to painful stimuli. Copious chemical data are presented on a

large number of psychotropic agents (438 refs.)

Pharmacological Laboratory
Roche Products Limited
Welwyn Garden City, Hertfordshire
Great Britain

2861 Peigné, F. Les médicaments psycholeptiques. [Psycholeptic treatments.] France Médicale, 1961, 1, 33-37.

Hypnotics, neuroleptics (or major tranquilizers) and tranquilizers (or minor tranquilizers)--all termed psycholeptics, are reviewed. The forms which are available in France of chlorpromazine, levomepromazine, acepromazine, methopromazine, prochlorperazine, thiopropemazine, thioridazine, reserpine, alimemazine and aminopromazine are detailed. The major neuroleptics used at low doses as tranquilizers are, principally, chlorpromazine, reserpine, levomepromazine and thioridazine. Miscellaneous tranquilizers listed are hydroxyzine, azacyclonol, captodiamine and meprobamate. The revolution these agents have effected in the treatment of psychoses is stressed. (No. refs.)

[No address]

2862 Masserman, Jules H., Kagen, Irving N., & Pauncz, Arpad. The neuroses. Progress in Neurology and Psychiatry, 1962, 17, 450-462.

Etiology, communication and symbolism, developmental and clinical signs, prognosis and therapy of the neuroses are reviewed. The use of LSD and chlordiazepoxide as adjunctive to psychotherapy, improvement on fluphenazine in patients suffering from anxiety, the use of isocarboxazid in neurotic and psychotic depression, and the efficacy of Elavil (amitriptyline and perphenazine) in endogenous depression are noted. (102 refs.)

[No address]

Reviews
Abstracts 2863-2868

2863 Jost, F., & Geertz, V. W. Modernos tratamientos en psiquiatría alucinógenos: Psicosis por LSD [Modern treatments in psychiatry; hallucinogens: LSD psychosis.] *Folia Clinica Internacional*, 1961, 11, 440-445.

The LSD experience (colored hallucinations, loss of time sense, etc.) and the use of LSD in postdelirium tremens patients, psychopaths and schizophrenics is reviewed, with brief mention of mescaline. (No refs.)

Neuropsychiatric Clinic
University of Innsbruck
Innsbruck, Austria

2864 Wikler, Abraham. Drug addiction. In: Baker, A. B. [Ed.] *Clinical Neurology*. Volume II. Minnesota: Hoeber-Harper, 1962. Pp. 1054-1083.

The clinical features, pathology, diagnosis, treatment, and rehabilitation of various drug addictions are outlined. Opiates and opioids, morphine, morphine mixtures and derivatives, synthetic analgesics (opioids), barbiturates, meprobamate and intoxications with marijuana, cocaine, amphetamine, and mescaline are detailed in textbook fashion. (142 refs.)

[No address]

2865 Hoeffler, Dennis F. Thalidomide. *Journal of Pediatrics*, 1962, 61, 483. [Letter]

A 40-year-old multipara with 2 normal children gave birth to a baby with typical thalidomide-induced phocomelia. Her history revealed thalidomide ingestion during the 1st trimester of pregnancy. Delivery took place in the U.S.A., but the drug had been obtained during overseas assignment in West Germany. (No refs.)

[No address]

2866 Taussig, Helen B. Phocomelia and thalidomide. *American Journal of Obstetrics and Gynecology*, 1962, 84, 979. [Letter]

Phocomelia appears wherever thalidomide is distributed, corroboration being found in several hundred cases of phocomelia in the

British Commonwealth, 25 in Sweden, several in Belgium, 5 in Italy, an epidemic in Brazil and numerous cases in Canada. Despite polyneuritis with chronic drug use, thalidomide would probably have been marketed in the U.S.A., had emphasis of its antiemetic properties in pregnancy not been heavily propounded in advertisements. The FDA did not think the agent proven safe in pregnancy. (No refs.)

Department of Pediatrics
Johns Hopkins University
School of Medicine
Baltimore, Maryland

2867 New Medical Materia. UK-738. *New Medical Materia*, 1962, 4, 41. [Editorial]

Grigyesi (Pownal, Me.) administered methylbenztropine (UK-738; 4-12 mg/day) to 84 patients with extrapyramidal disorders, 54 of whom had been receiving trihexyphenidyl and benztropine. Methylbenztropine appeared to be a weaker antiparkinsonian drug than either of the controls, but its effectiveness against rigidity and lack of side effects made it valuable as an addition to the management of the 37 patients with parkinsonism. In 39 patients with athetosis, 6 with tremor and 2 with myoclonus, methylbenztropine exerted a clear therapeutic effect in contrast to control drugs. (No refs.)

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New York 19, New York

2868 New Medical Materia. Dexedrine. *New Medical Materia*, 1962, 4, 36. [Editorial]

Fish (Costa Mesa, Calif.) administered dexamphetamine (1 capsule/day or placebos) to 106 mentally retarded patients with speech defects for 3 months. Only stutterers improved, and 5 of the 11 treated with dexamphetamine showed improvement as compared with 1 of the 11 patients treated with placebos. Three stutterers improved so dramatically that their stuttering was controlled to the point of obviation. Side effects included 2 with increased psychotic disturbances, 2 with increased athetosis and 2 with excessive weight loss. (No refs.)

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2869 Berzel, Nicholas, A. What have we learned from LSD? Archives of Neurology, 1962, 6, 85-86.

LSD has contributed substantially to understanding certain psychotic symptoms by enabling the observer to experience the subjective setting of psychosis. It is also efficacious in psychotherapy, despite interference by suggestion in some transcendental experiences. LSD should not be misused in the manner of amobarbital or ether to elicit abreactions. Currently mescaline is favored over goof balls or benzedrine for producing a temporary jag. (No refs.)

[No address]

2870 Norris, A. S. Current treatment of depression. Journal of Iowa Medical Society, 1962, 52, 594-597.

Older drugs used to combat mild depressions include amobarbital, amphetamine, dexamphetamine, methylphenidate, etc. Newer drugs designed to ameliorate all types of depressions include imipramine, amitriptyline and the MAO inhibitors (phenelzine, nialamide, isocarboxazid, tranlycypromine and etryptamine). Depression should be diagnosed and evaluated with an eye toward potential suicidal tendencies. (2 refs.)

State University of Iowa
College of Medicine
Iowa City, Iowa

2871 Fisher, Terrance N. Current concepts of monoamine oxidase inhibitors. Marquette Medical Review, 1962, 27, 86-95.

A review of MAO inhibitors encompasses the pharmacology and types of MAO inhibitors. Clinical responses include antidepressant effect, increased pain threshold, effect on mesenchymal tissues, appetite stimulation, antianginal effect and antihypertensive effect. Toxicity reactions, albeit rare, include mental confusion, agitation, hallucinations, anemia and skin rashes, but by far

the most serious complication is acute liver necrosis. MAO inhibitors available currently include iproniazid, phenelzine, isocarboxazid, pheniprazine, nialamide, and tranlycypromine. Theories for antianginal and antihypertensive effects are elaborated. (55 refs.)

Marquette University School of Medicine
Marquette, Illinois

2872 Bente, D. Remarks on modern German psychiatry. Diseases of the Nervous System, 1962, 23, 32-35.

The University "Nervenklinik" at Erlangen handles 1200 patients/year, usually on an outpatient basis. Contemporary German psychiatry still derives from Kraepelin's classifications although it has progressed to include Gestalt psychology, phenomenology, Kretschmer's multidimensional diagnosis and therapy and, of course, Sigmund Freud. Much emphasis has also been placed upon ECT, insulin coma, chlorpromazine and other psychotropic drugs. Psychopharmacology will open new vistas in German psychiatry. (No refs.)

Universitäts-Nervenklinik
Erlangen, Germany

2873 Fleck, Stephen. Residential treatment of young schizophrenics. Connecticut Medicine, 1962, 26, 369-376.

At the Yale Psychiatric Institute, a private 44-bed intensive treatment, psychodynamically oriented hospital, the treatment program may be divided into 2 parts: intensive psychotherapy and the therapeutic community. In addition, tranquilizing drugs are sometimes used, particularly early in treatment. About 25% of the patients receive tranquilizers and about 40% are on night sedation. Shock therapy was being used with only 1 patient in the last 2-2.5 years. Further, a program of activities, athletics, occupational therapy, education, and work is available according to the needs of the individual patient. Two-thirds of 85 schizophrenics discharged in a recent 5-year period have adjusted with some success. (28 refs.)

Yale University School of Medicine
New Haven, Conn.

Reviews
Abstracts 2874-2878

2874 Geyer, Karl-Heinz. Über das Prinzip der therapeutischen Wirkungsumkehr psychotroper Substanzen. [The principle of reversal of therapeutic effect of psychoactive agents.] Therapie der Gegenwart, 1962, 6, 286-292.

Based on clinical and laboratory reports and the experience gained with 1 patient, specific conditions are discussed which may lead to a reversal of the expected effect of administered psychopharmacological agents, e.g. chlorpromazine and imipramine. The biologic reactions may be similar in spite of a pharmacologic antagonism (neuroleptic-thymoleptic); the direction of the therapeutic effect is determined by the individual initial mental stage of the patient rather than by the specificity of the psychotropic agent. The "toxic aggression" effect of the drug, and changes in customary dosages are factors which contribute to the occurrence of this reversal. (14 refs.)

Neurologische Abteilung der Städt. Krankenhäusern
Aachen, Germany

2875 Petroff, Cottbus. Aus der internationalen Fachliteratur. Korsakow-Zeitschrift für Neuropathologie und Psychiatrie, 1962, Heft 1. [From the international medical literature. Korsakow-Journal for Neuropathology and Psychiatry, 1962, [No. 1.] Arzneimittel-Forschung, 1962, 12, 385-388.

After briefly summarizing German government directives for research in the field of neuropathology and psychiatry, the reviewer presents abstracts of 22 articles. Twelve papers deal with circulatory disturbances, mostly of the CNS, the remaining with different forms of psychoses and/or neuropsychiatric disorders. (12 refs.)

[No address]

2876 Grant, Quentin Rae. Psychopharmacology in childhood emotional and mental disorders. Journal of Pediatrics, 1962, 61, 626-637.

Psychopharmacologic agents provide symptomatic help without ameliorating underlying problems in childhood psychiatric distur-

bances. However, the amphetamines are advocated for ailments of organic or even mildly neurotic origin. Acute emergencies and severe emotional disorders respond optimally to phenothiazines like chlorpromazine. Reserpine is also widely applicable and efficacious. Mildly disturbed children may respond to meprobamate therapy in the behavioral disturbances. (75 refs.)

Department of Pediatrics and Psychiatry
Johns Hopkins University
Baltimore, Maryland

2877 Mandel, Arnold, Markham, Charles H., & Fowler, William. The use of Tofranil in the treatment of Parkinson's disease. Archives of Neurology, 1962, 6, 81; discussion 31-85.

Administration of imipramine (Tofranil; 250 mg/day) to patients with Parkinson's disease revealed mild benefit, no benefit, or in 6 with severe akinesia, considerable increase in activity. Of these, 3 showed considerable alleviation of depression while the rest exhibited only improvements in physical state. An extensive discussion is included. (No refs.)

[No address]

2878 Schmidt, Georg. Forensisch wichtige Fragen der Barbiturat-Ausscheidung im Harn. [Problems of forensic importance regarding the urinary barbiturate-excretion.] Arzneimittel-Forschung, 1962, 12, 1081-1085.

Intensity and course of action differs widely in various barbiturates. Therefore, conclusions concerning the effect may be drawn only if the drug has been specifically identified and quantitatively determined. The evaluation of small quantities of blood and urine for quantitative determination of barbiturates and their metabolites are complicated and time-consuming. Whenever possible the results should be checked by paper chromatography, spectrophotometry and crystal-optic methods. From the investigation of the urine important conclusions may be drawn

concerning the amount of the drug ingested and the time of administration. If 2 or more barbiturates, or barbiturates combined with alcohol have been ingested, the maximal effect of each drug must be accounted for. Synergistic effects of small doses may be expected. Such information is important in the assessment of impaired driving ability. (41 refs.)

Institut für gerichtliche Medizin und Kriminalistik
Universität Erlangen-Nürnberg
Erlangen, Germany

2879 Aring, Charles D., The riddle of the Parkinson syndrome. Archives of Neurology, 1962, 6, 1-4. [Editorial]

Parkinson's disease may be ameliorated with almost any compound in about 50% of the patients for varying periods of time. Etiology is elusive and enigmatic, with medication administered on a trial and error basis. A certain personality rigidity (ego-defenses, suppressed motor aggressiveness) appears to predispose toward parkinsonism. The phenothiazines failed to offer elucidation of muscular rigidity or involuntary movements, despite the fact that such side effects occur in about 15% of cases treated with phenothiazine derivatives. (14 refs.)

Department of Neurology
University of Cincinnati College of Medicine
Cincinnati, Ohio

2880 Neuman, Maur. Neuroleptics. Concours Médicale, 1962, 84, 4519-4524.

The pharmacology of neuroleptics and their clinical uses are reviewed, largely by chemical type, i.e., a) dimethylaminopropyl side chain (chlorpromazine, promazine, methylpromazine, propylolazine, acetylpromazine, etc.), b) piperazine side chain (chlorpromazine, prochlorperazine, properazine, trifluoperazine, etc.), c) piperidinic side chain (mepazine and thiordazine), thiozanthine derivatives (prothixene, prochlor-thixene), azephenothiazines (protypendyl), butyrophenones (haloperidol), and benzoquinolizines (tetrabenzine. (29 refs.)

[No address]

2881 German Medical Monthly. The occurrence of dopamine (3-hydroxytyramine) in the central nervous system: its relationship to parkinsonism. German Medical Monthly, 1962, 7, 344-346.

The physiological importance of dopamine for the functioning of the extrapyramidal system is suggested by the distribution of dopamine in this system in animal experiments, and by the effect of L-DOPA on akinesia in parkinsonism, in which the neostriatum is depleted of dopamine. Although of considerable theoretical interest, the therapeutic value of L-DOPA in parkinsonian akinesia is not definitely established. Studies in changes in dopamine, leverteranol and 5 HT in the brains of patients who died of Parkinson's disease and of postencephalic parkinsonism showed the following: in the parts of the brain which are normally rich in these amines, reduced levels were found in cases of parkinsonism. Dopamine was particularly reduced in the caudate nucleus and the putamen, i.e., in structures of the extrapyramidal motor system (41 refs.)

[No address]

2882 Bukiet, V. Embryopathies caused by thalidomide. Concours Médicale, 1962, 84, 3999-4000.

The literature on thalidomide syndrome, with an emphasis on German work, is reviewed. (12 refs.)

[No address]

2883 Neuman, Maur. Psychotonics (Psycholeptics). Concours Médicale, 1962, 84, 4911-4920.

Thymoleptics (MAO inhibitors, imipramine) psychotonics such as centrophenoxine, stimulants like the amphetamines and convulsive central excitants such as bemegride are reviewed. Hormones, antigens and glucocorticoids are briefly noted. Criteria for the choice of a psychotonic in the treatment of ambulatory patients are outlined. (49 refs.)

[No address]

Reviews
Abstracts 2884-2889

2884 Nature. Comparative neurochemistry. Nature, 1962, 195, 443.

The 5th International Neurochemical Symposium was held at St. Wolfgang, Austria during June 11-15, 1962 and the topic chosen was Comparative Neurochemistry. Available data on differences in structure, chemical composition, metabolism, enzymatic activity and drug and hormone effects on the CNS of invertebrate and vertebrate species were discussed on an interdisciplinary basis. (No refs.)

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London, W.C. 2, Great Britain

2885 Nature. Addiction-producing drugs. Nature, 1962, 195, 1154. [Editorial]

Continuing its work of notification, the WHO Expert Committee on Addiction-producing Drugs recommends in its 12th report exemption from the provisions of international control for oxpheneridine, (-)-3-hydroxy-N-propargyl-morphinan, methethoheptazine, methheptazine, and 2 preparations of diphenoxylate, (Technical Report Series No. 229: Pp. 16. Geneva, WHO), and 4 diphenoxylate preparations. On the other hand, noracetymethadol is considered to be an addiction-producing drug comparable with morphine, while nicocodine and the 4 compounds designated by the committee as methadone-intermediate moramide-intermediate, pethidine-intermediate-A and pethidine-intermediate-B are all found to be convertible into addiction-producing drugs and therefore subject to the relevant provisions of international control. Concern is expressed about continuing traffic in heroin, which has been more available than opium. The controls on the illicit production of heroin and on the traffic in this drug need to be enforced more strictly. The Committee noted that the Single Convention of Narcotic Drugs, drawn up in 1961, affords the WHO the opportunity to initiate the examination of dangerous drugs and adapt the extent of control to the degree of hazard to public health. (No refs.)

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London, W.C. 2, Great Britain

2886 Dauchy, F. Monoamine oxydase inhibitors. Concourse Médicale, 1962, 84, 2257-2259.

The pharmacology, psychiatric use, toxicity and principal MAO inhibitors are reviewed. Phenelzine, Tersavide, isocarboxazid, pheniprazine, iproniazide, nialamide, and serine-N2-isopropyl-hydrazide are noted. (1 ref.)

[No address]

2887 Darling, Harry F. Phenmetrazine HCl addiction. American Journal of Psychiatry, 1962, 119, 84.

The author cites omissions of references in his article "Addiction to Phenmetrazine HCl" which appeared in the American Journal of Psychiatry, 1961, 118, 6, particularly noting J. A. Rosen's paper which appeared in the Journal of the American Osteopathic Association in 1959. (1 ref.)

Kannan Building
Lawrence, Massachusetts

2888 Wolfle, Dael. The thalidomide lesson. Science, 1962, 137, 497. [Editorial]

Dr. Kelsey's caution (FDA) has prevented much heartache, and it appears that the thalidomide case may be useful in improving the procedures used in evaluating and appraising new drugs. However, restrictions could be made which would be severe enough to impede the development and use of new and beneficial drugs. (No refs.)

Science
1515 Massachusetts Avenue, N.W.
Washington 5, D. C.

2889 Barbeau, André. La maladie de Parkinson. [Parkinson's disease] Union Médicale du Canada, 1962, 91, 539-540.

After noting that about 1 person out of 200 dies with signs related to Parkinson's disease, it is postulated that (after Kurland et al.) approximately 30% of the general population carries the abnormal recessive

one which is responsible. This figure corresponds closely to the incidence of extrapyramidal complications 1 out of 3 in a group of over 1500 patients receiving phenothiazines at Ayd's clinic. A deficiency in dopa-decarboxylase is possibly involved. (No refs.)

[No address]

2890 Insua, Jorge A. Psicofarmacos en la depresion. [Psychopharmaka in depression] Prensa Medica Argentina, 1962, 49, 965-971.

The use of MAO inhibitors, phenothiazine derivatives, antidepressants and stimulants, and tranquilizers in the various types of depression (hysteric and obsessive, reactive, evolutionary, schizophrenic, symptomatic, and those caused by organic psychoses) is outlined. (No refs.)

Instituto de Semiología
Hospital de Clínicas
Buenos Aires, Argentina

2891 New Medical Materia. Under clinical study. New product concepts and new uses of old products. New Medical Materia, 1962, 4, 41. [Editorial]

Information is presented on 6 drugs, 2 of which are psychoactive: pargyline and UK 738. Pargyline has been confirmed as an effective antihypertensive agent, while the anticholinergic UK 738 (methylbenztropine) has been found useful in the control of extrapyramidal disorders. It appears weaker than trihexphenidyl and benztropine, but is effective against rigidity and well tolerated. (No refs.)

New Medical Materia
Hearst Corporation
1790 Broadway
New York 19, New York

2892 New Medical Materia. The thalidomide nightmare, 1962, 4, 5-6. [Editorial]

Among the demands brought forth relating to the thalidomide situation are: prompt exchange of international pharmacological information on new drugs with emphasis on side

effects, more stringent procedures governing the selection of physicians permitted to experiment with new drugs, liberalization of state abortion laws, limits to the number of patients to be given experimental drugs, cooperation among government agencies in recording and classifying drug data, selection of many more hospitals to engage in cooperative research on unfavorable side reactions, crackdown on doctors suspected of rigging research on new drugs, creation of an impartial committee of medical scientists to select researchers for new drugs, compulsory use in drug testing of pregnant animals, submittal to FDA of all reports on the outcome of animal tests, termination of clinical testing by FDA if doubts arise as to safety, federal clearance for the importation of new drugs by doctors and confiscation by the Post Office of unapproved drugs entering country. (No refs.)

Hearst Corporation
1790 Broadway
New York 19, New York

2893 New Medical Materia. A concerted attack on narcotics, New Medical Materia, 1962, 4, 7. [Editorial]

Celebrezze's remarks at the 1st White House Conference on narcotic and drug abuse clearly underscore the tough, unyielding complexities of narcotic addiction. New York State's Metcalf-Volker law, the National Council for the Prevention of Addiction to Narcotics and recent federal legislation are discussed. (No refs.)

Hearst Corporation
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New York 19, New York

2894 New Medical Materia. The narcotics problem is tough. New Medical Materia, 1962, 4 5-6. [Editorial]

The narcotics problem, involving 60,000 known addicts in the United States, is discussed in relation to reasons why society wants the addict cured contrasted against the addict's need to escape reality (91% relapse from cure), and the painful withdrawal symptoms involved in cure. Pros and cons of the "no compulsory treatment" and the

"compulsory treatment" are discussed. (No refs.)

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2895 Nature. Chemistry and mental disease.
Nature, 1962, 195, 439. [Editorial]

A symposium on "Chemistry and Mental Disease" arranged by the Royal Institute of Chemistry, the Chemical Society, and the Society of Chemical Industry was held at the University of Manchester on September 26, 1962. The program included biochemical processes in relation to mental disease (Todrick), inborn metabolic errors and mental disease (Woolf), pharmacologic assessment of psychotropic activity (Parkes), tranquilizers--structure and activity relationships (Crowther), psychostimulants--structure and activity (Young) and values of modern drugs in psychiatric practice (Jenner). (No refs.)

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2896 Medical World News. World experts view thalidomide. International conclave suggests drug's effect on the human embryo could not have been predicted despite the most thorough experimental testing. Medical World News, 1962, 3, 68, 70. [Editorial]

The consensus of opinion gathered from the 10th International Congress of Pediatrics in Lisbon was that the thalidomide tragedy could not have been avoided. However the catastrophe revealed how poor the existing warning system was. In Germany, the lay press turned out to be the most efficient warning system. Phocomelia is the most common malformation produced. (No refs.)

Medical World Publishing Co, Inc.
30 Rockefeller Plaza W.
New York 20, New York

2897 Laurent, J. M. Toxique et toxicomanie peu connus, "le cath." [A little-known poison and toxicomania, khat.] Annales Médico-Psychologiques, 1962, 120, 2, 649-657.

Khat, from *Catha edulis*, contains 3 alkaloids, namely cathinine, cathidine and cathine. The last is d-norisoephedrine, while the first 2 are very similar to ephedrine. The extract provokes tachycardia, vasoconstriction, hypertension, digestive atonia, insomnia and anorexia. It can paralyze the digestive tract causing paralysis of the ileum. Psychic effects are not in the form of a specific syndrome, but generally include insomnia, impotence, excitomotor seizures, outbursts of delirium. Social consequences of its abuse in Arabic countries and eastern Africa are discussed. (15 refs.)

Hopital Peltier
Djibouti, French Somaliland

2898 Lowenbach, Hans, Green, Robert L. & Verwoerd, Adriaan. Clinical psychiatry, Progress in Neurology and Psychiatry, 1962, 17, 390-411.

The effectiveness of modern psychotropic drugs has allowed modifications in mental hospitalization leading to the open door policy, e.g., St. Lawrence (N.Y.) State Hospital has been open since 1956, and increases the feasibility of home care programs. Some of the current biochemical factors in mental illness, especially schizophrenia are discussed, e.g., the work of Altschule (i.e., Veech et al. 1961), i.e., urinary aminochromes from adrenolutin and adrenochrome identified in the urine of schizophrenics (186 refs.)

[No address]

2899 Naranjo, Plutarco. Effets secondaires et structure chimique des tranquillizants. [Side effects and chemical structure of tranquilizers.] Médecine et Hygiène, 1962, 20, 783-789.

The side effects of tranquilizers (behavioral CNS, autonomic nervous system disorders, cardiovascular, blood, metabolic, endocrine and hepatic disorders, and allergic manifestations) are discussed in relation to phenothiazine derivatives, reserpine group of tranquilizers, diphenylmethane derivatives, carbamic derivatives and miscellaneous compounds. Drowsiness and hypotension seem

characteristic, and frequently anticholinergic effects are noted. The occurrence of drowsiness, extrapyramidal disorders and atropinelike side effects, and blood dyscrasias for a large number of tranquilizers is given. (No refs.)

No address]

2900 Sussex, James N. Drugs used in psychiatric treatment. II. Medical Record and Annals, 1962, 55, 245-247, Passim.

The use of drugs in psychiatric disorders is almost entirely on an empirical basis. However, the appearance of effective tranquilizers and antidepressants has been a boon to psychiatry and medicine in general. Emotional disturbances are considered in 2 categories: anxiety and agitation in 1, and depression in the other. Tranquilizers as represented by reserpine and most of the phenothiazines are of use in the anxiety-agitation syndrome while methylphenadate, piperdol, and drugs of the amphetamine series are useful in very mild depression of recent origin, and the MAO inhibitors, imipramine, and iproniazid are valuable in the treatment of more severe and definitely depressive illnesses. (No refs.)

Department of Psychiatry
University of Alabama School of Medicine
Birmingham, Ala.

2901 Lembeck, F. & Zetler, G. Substance P—a polypeptide of possible physiological significance, especially within the nervous system. In: Pfeiffer, Carl C. & Smythies, John R. [Eds.] International Review of Neurobiology. Volume IV. London: Academic Press, Inc., 1962. Pp. 159-215

Extraction, estimation, purification, enzymatic destruction, chemical properties of substance P and the differentiation of it from other smooth-muscle stimulants, especially polypeptides, are described. Substance P distribution in the gastrointestinal tract (high in the duodenum and jejunum), CNS (human brain cortical tissue of the anterior cingulate gyrus is ca. 85 U/g which is significantly greater than the concentration in the precentral ca. 43 U/g) and the peripheral nervous system is given. Sub-

stance P concentrations in whole brain and forebrain, as well as brainstem are given for some 26 species of animals. Relationship between organ function and tissue concentration of substance P in the intestines, CNS and degenerating nerve, and its postulated role as a transmitter substance of sensory nerves are detailed. The necessity of obtaining pure substance P preparations before attributing a central transmitter role to the substance is emphasized. (173 refs.)

Department of Pharmacology
University of Graz
Austria

2902 Abood, L. G., & Biel, J. H. Anticholinergic psychotomimetic agents. In: Pfeiffer, Carl C., & Smythies, John R. [Eds.] International Review of Neurobiology. Volume IV. London: Academic Press, Inc., 1962. Pp. 217-273.

A number of piperidyl glycolate esters have been found to produce hallucinations and other profound behavioral disturbances in humans. Emphasis is placed upon the structure-activity relationships of this class of agents and a possible mode of action on neuronal and other excitable systems. These agents may be classified into the following groups: Group I—esters of substituted glycolic acid derivatives and heterocyclic amino alcohols; Group II—esters of substituted glycolic acid derivatives and substituted piperazino alcohols; Group III—miscellaneous analogues of I and II. Gross effects in rats, sequential response in rats and behavioral effects in humans are reviewed. Neurological-autonomic (side effects) are listed. Psychological studies in humans have included comparisons to other agents such as LSD in various tests, e.g., MMPI, Jarvik Questionnaire, Clyde Mood Scale and the Rorschach Test. Phenothiazines and other tranquilizers, as well as d-tubocurarine, phenobarbital and other agents are antagonists to piperidyl glycolates (antagonism to hyperactivity in rats). Clinical studies with the glycolate esters and biochemical and electrophysiological studies with piperidyl glycolate, including effects on enzyme systems, metabolic effects in frog nerve and muscle, possible mechanism for biochemical effects, effects on contractile and excitable systems of frog sartorius muscle and the applicabil-

ity of piperidyl glycolates to studying biochemical, functional relationships are surveyed. (62 refs.)

Departments of Psychiatry and Biological Chemistry
University of Illinois
Chicago, Ill.

2903 Pletscher, A., Brossi, A., & Gey, K.F. Benzoquinolizine derivatives--a new class of monamine decreasing drugs with psychotropic action. In Pfeiffer, Carl C., & Smythies, John R. [Eds.] International Review of Neurobiology. Volume IV. London: Academic Press Inc., 1962. Pp. 275-306.

Present knowledge on the chemistry, metabolism, biochemistry, pharmacology and clinical effects of benzoquinolizines and the relationship between changes of monoamine metabolism and pharmacological action in relationship to the benzoquinolizine are reviewed. Tetrabenazine (75-150 mg/day) is particularly beneficial in relieving hallucinations and paranoid symptoms of schizophrenia. It appears effective in euphoric hebephrenia with superimposed mania and also has been found beneficial in Huntington's chorea. Side effects of tetrabenazine are generally similar to those of reserpine, but rather less severe. Several benzoquinolozines decrease 5HT and catecholamines contents preferentially in the brain. They are potent but short acting. MAO inhibitors antagonize or reverse several of these effects. Compounds discussed are given in the table below:

Code No.	Substitution	Formula
Ro 1-9288	2-Hydroxy-3-n-butyl-9,10-dimethoxy-	Va
Ro 1-9564	2-Hydroxy-3-ethyl-9,10-methylendioxy-	Va
Ro 1-9569	2-Oxo-3-isobutyl-9,10-dimethoxy- (= tetraben-zine, Nitoman)	IVb
Ro 1-9571	2-Hydroxy-3-isobutyl-9,10-dimethoxy-	Va
Ro 4-0786	2-Hydroxy-2-ethinyl-3-ethyl-9,10-dimethoxy	VIa
Ro 4-1284	2-Hydroxy-2-ethyl-3-iso-butyl-9,10-dimethoxy	VIa
Ro 4-1286	2-Hydroxy-2-ethyl-3-n-butyl-9,10-dimethoxy-	VIa

Ro 4-1374	2-Hydroxy-2-allyl-3-iso-butyl-9,10-dimethoxy-	VIb
Ro 4-1376	2-Hydroxy-2-isobutyl-3-ethyl-9,10-dimethoxy-	VIb
Ro 4-1398	2-Hydroxy-2-(3-methoxy-butyl)-3-isobutyl-9,10-dimethoxy-	VIb
Ro 4-1632	2-Oxo-3-(2-ethylbutyl)-9,10-dimethoxy	IVb
Ro 4-1860	2-Hydroxy-2-ethyl-3-(2-ethylbutyl)-9,10-dime-thoxy	VIa

Tetrabenazine prevents reserpine-induced sedation. Some benzoquinolozine derivatives may cause moderate hypotension, probably unrelated to monoamine depression. (86 refs.)

Research Departments
F. Hoffmann-LaRoche & Co., Ltd.
Basel, Switzerland

2904 Hoffer, A. The effect of adrenochrome and adrenolutin on the behavior of animals and the psychology of man. In: Pfeiffer, Carl C., & Smythies, John R. [Eds.] International Review of Neurobiology. Volume IV. London: Academic Press Inc., 1962. Pp. 207-371.

The biochemistry of adrenochrome, its action on cells, fish, spiders, pigeons and mammals, its effect on electrograms, the effect of adrenochrome and adrenolutin on humans, and its mode of action are discussed. Adrenochrome and adrenolutin produce marked changes in the behavior of animals with the finer aspects of behavior altering first. Gross changes are produced only by large quantities. The types of change produced in humans mimic in many ways the changes seen in schizophrenia. The kind of visual hallucinations seen with mescaline, LSD, psilocybin and other substances is not produced. The basic issue is whether or not adrenochrome and compounds which can be derived from it in vivo, perhaps adrenolutin and 5,6-dihydroxy-N-methylindole, are active hallucinogens in man. Evidence is gathering that these compounds do exist in the body. (190 refs.)

Psychiatric Services Branch
Department of Public Health
Saskatoon, Saskatchewan
Canada

2905 Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 1-477.

This book covers the following topics: the pharmacologists of Edinburgh; highlights of pharmacology in Middle China; highlights of pharmacology in India; highlights of pharmacology in Central Europe; biochemical mechanism of drug action; the relationship between chemical structure and pharmacological activity; mechanisms of drug; invertebrate pharmacology--selected topics; parasite chemotherapy; sites of action of some CNS depressants; drugs affecting the blood pressure and vasomotor tone; renal pharmacology; pharmacological control of adrenocortical and gonadal secretions; toxicology--inorganic; the smaller halogenated hydrocarbons; recent developments in chemical and biochemical assay techniques applicable in pharmacology, and it supplies a review of reviews. (3,342 refs.)

Stanford University School of Medicine
Palo Alto, California

2906 Mukerji, B., De, N.N., & Kohli, J.D. Highlights of pharmacology in India. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 17-30.

Indian research on drugs acting on the sensory peripheral nervous systems is presented. The stimulant qualities of 2-piperidyl-(1)-3 phenyl propanol, the hypnotic activity of 2,3-disubstituted quinazalone, and the anticonvulsant action of bromide are discussed. A specific antagonism has been shown to exist between LSD and morphine, and related drugs. Reserpine emesis is prevented by LSD, caffeine, iproniazid, methamphetamine, morphine, rauwolscine and yohimbine in pigeons. Following the success of rauwolfia, a number of plants have been studied for similar properties, e.g., Nardostachys jatamansi, Acorus calamus, Wythania somnifera, W. ashwagandha, etc. Herpestis monniera has been shown to potentiate barbiturate and alcohol hypnotic effects. A related plant, Hydrocotyle asiatica has only weak sedative action. The quaternary salt

of hayatin, an alkaloid isolated from Cissampelos pareira has been shown a potent neuromuscular blocking agent. (167 refs.)

Central Drug Research Institute
Lucknow, India

2907 Rasková, Helena. Highlights of pharmacology in Central Europe. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology Volume II. Palo Alto: Annual Reviews, Inc. 1962. Pp. 31-36.

Pharmacological research in Czechoslovakia, Hungary and Poland is reviewed under the headings: CNS; pharmacology of the heart; pharmacology of lipid metabolism; atherosclerosis; anticoagulants; antibiotics; radiopharmacology, and information, non-specific resistance and toxins. N-3-diethylaminopropyl homacridine HCl, proheptadien, chlorproheptatrien and chlorproheptadien have antidepressant effects. 2-Piperidino-methyltetralon-1 has major tranquilizing properties; some of the β -amino-ketones have anticonvulsant properties and potentiate the tranquilizing effect of reserpine but antagonize its influence on electroshock. A new drug, 1-piperidino-1-methyl-3-(ptolyl)-propan-3-on has demonstrated interneuron-depressing activity. Information on chronic reserpine treatment and adaptation to external stimuli in dogs is presented. Chlorpromazine and other tranquilizers inhibit in vitro oxidative phosphorylation and ATP activity. The uncoupling effect of chlorpromazine is bound mainly to the subthalamic region, more specifically than the barbiturates. Tranquilizing activity can be predicted from in vitro experimentation. The importance of chlorpromazine as a central antagonist of local anesthetics in premedication has been emphasized. Long-lasting increase of electrical activity after a marked latency has been demonstrated by injecting epinephrine levarterenol and MAO inhibitors directly into the reticular formation. Further information on phenothiazines and CR suppression is present. (86 refs.)

Department of Pharmacology
Charles University
Prague, Czechoslovakia

Reviews
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2903 Bain, J. A., & Mayer, S. E. Biochemical mechanisms of drug action. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 37-66.

This review covers chlorpromazine effects on d-amino acid oxidase, effects of chlorpromazine on mitochondrial respiration and coupled phosphorylation, barbiturates, ethyl alcohol, salicylates, MAO inhibitors, GABA, vitamin B₆ and hydrazines, orally active hypoglycemic drugs, the effects of catecholamines and adrenergic blocking agents, anticoagulants, carbonic anhydrase inhibitors, the cytochemical effects of drugs and poisons in the liver, including antihistaminics and neuromuscular blocking agents, trialkyltin, antibiotics, insecticides and antiparasitic agents, protoveratrine and cocaine, and local anesthetics. (207 refs.)

Department of Pharmacology
Division of Basic Health Sciences
Emory University
Atlanta 22, Georgia

2909 Bloom, B. M., & Laubach, G. D. The relationship between chemical structure and pharmacological activity. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 67-108.

Structural parameters pertinent to biological interactions of drugs are reviewed. The size, shape and electron distribution of promazine and promethazine in relation to Fisher-Hirschfelder-Taylor models, the binding of 5HTP and DOPA to aromatic amino acid decarboxylase, formulas of pethidine analogues, absorption and distribution of drugs, localization of drugs in tissues, special transport mechanisms, metabolic transformations, structure and actions at receptors, Belleau's adrenergic receptor model and other topics are elucidated. (249 refs.)

Medicinal Chemistry Department
Chas. Pfizer and Company Inc.
Medical Research Laboratories
Groton, Connecticut

2910 Rall, David P., & Zubrod, C. Gordon. Mechanisms of drug absorption and excretion. Passage of drugs in and out of the central nervous system. In: Cutting, Windsor, C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 109-128.

Methodological considerations and the pharmacological anatomy of the CNS including the formation and flow of CSF are reviewed with emphasis on the exchange of compounds between blood, CSF and brain. Drugs can exchange between the brain or CSF by either diffusion or some form of active transport. Exit of drugs from the CSF is aided by a 3rd mechanism, bulk flow. The choroid plexus represents a solid cellular layer as a barrier between blood and CSF. The capillary wall completely surrounded by glia and other cellular elements presents a cellular barrier between blood and brain. (125 refs.)

Clinical Pharmacology and Experimental
Therapeutics Service
National Cancer Institute
NIH
Bethesda, Maryland

2911 Boyland, E. & Booth, J. The metabolic fate and excretion of drugs. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 129-142.

Hydroxylation (ring hydroxylation and N-hydroxylation), the biosynthesis of glucuronides, the role of phosphoric esters as metabolites of foreign compounds and the effect of carcinogens on microsomal enzymes are reviewed. The conversion of zoxazolamine into chlorzoxazone in man and the conversion of the depressant butamoxane to 6- (or 7-) hydroxybutamoxane by rats and dogs are detailed. Also the metabolism of nicotine by rat liver is reviewed. (84 refs.)

Chester Beatty Research Institute
Institute of Cancer Research
Royal Cancer Hospital
London, Great Britain

2912 Crescitelli, Frederick, & Geissman, T. A. Invertebrate pharmacology--selected topics. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 143-192.

Bioassay methods (e.g., for catecholamines), the pharmacological analysis of transmitting mechanisms (especially the effects of acetylcholine, epinephrine, eserine, atropine, the curares and pharmacologically related drugs), cholinergic mechanisms, acetylcholine, noncholinergic systems, catecholamines, 5HT and indolylalkylamines, compounds of invertebrate origin, etc., are reviewed. (416 refs.)

Departments of Zoology and of Chemistry
University of California
Los Angeles, California

2913 Domino, Edward F. Sites of action of some central nervous system depressants. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 215-250.

This detailed review deals largely with the neural mechanisms of action of barbiturates, meprobamate, chlordiazepoxide, morphine, chlorpromazine and reserpine. (175 refs.)

Department of Pharmacology
University of Michigan
Ann Arbor, Michigan

2914 Smelik, Pieter G., & Sawyer, Charles H. Pharmacological control of adrenocortical and gonadal secretions. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 313-340.

Pharmacological agents exerting their influence entirely via the CNS, adrenal and gonadal secretions, humoral control of pituitary secretion, effects of hormones (pituitary-adrenal axis and pituitary-gonad axis), the effects of corticotropic hormones on target organs (adrenals and gonads), adrenal cortex inhibitors, antifertility agents and aldo-

sterone are reviewed. Within these frames of reference, the effects of perphenazine, nalorphine and morphine, ether and pento-barbital, reserpine, chlorpromazine, epinephrine and phenytoin are detailed. (326 refs)

Department of Anatomy and Brain Research
Institute
University of California School of Medicine
Los Angeles, California

2915 Maickel, R. P., & Weissbach, H. Recent developments in chemical and biochemical assay techniques applicable in pharmacology. In: Cutting, Windsor C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 399-414.

Spectrophotofluorometry, gas chromatography and new developments in radioisotope techniques are expounded. The basic components of the spectrophotofluorometer are a high-intensity xenon arc source which emits continuously throughout most of the UV and visible regions and 2 diffraction-grating monochromators, 1 to separate monochromatic light for excitation and a 2nd monochromator at right angles to analyze the emitted fluorescence. A photomultiplier circuit measures the intensity of fluorescence. Its use in the assay of tryptophan and its metabolites is detailed. The assay of 5HT and related compounds (e.g., 5HTAA), is reviewed. The applications of gas-liquid chromatography for steroids, amino acids and derivatives, drugs and miscellaneous compounds (e.g., imipramine), tritium gas exposure labeling and the application of liquid scintillation counting techniques are explained. (119 refs.)

Laboratory of Chemical Pharmacology
National Heart Institute
NIH
Bethesda, Maryland

2916 Leake, Chauncey, D. Reviews of reviews. In: Cutting, Windsor, C., Dreisbach, Robert H., & Elliott, Henry W. [Eds.] Annual Review of Pharmacology. Volume II. Palo Alto: Annual Reviews, Inc., 1962. Pp. 415-430.

Review material is given on basic pharmacological problems, practical sociological aspects of current pharmacology, pharmacological aspects of metabolism, chemical disinfection and chemotherapy of infectious diseases, autonomic drugs, CNS stimulants and depressants, psychopharmacology, cardiovascular drugs, enzymes, proteins and hormones, toxicology and miscellany. Analeptics have been reviewed by Hahn (1960.) Sideman (1961) surveyed 204 references on the clinical pharmacology of hypnotics and sedatives. Eckenhoff and Oech (1961) reviewed 262 contributions dealing with the effects of narcotics and narcotic antagonists of respiration and circulation in humans. Telford and Keats (1961) reviewed narcotic and narcotic-antagonist mixtures. Way and Adler (1960) reviewed 338 references bearing on the metabolic fate of morphine and its surrogates. Callaway and Stone (1960) offered a critical review of psychopharmacologic theory. The placebo effect has been carefully analyzed by Loranger, Prout and White (1961). Roth and Barlow (1961) reviewed the penetration of drugs into the brain, using autoradiography. Bures (1960) has reviewed the spreading depression phenomenon following the local application of salt solutions to various parts of the brain as first described by Leao. Impastato (1959) introduced a critical symposium on nialamide and Brill (1961) a symposium on chlordiazepoxide. (91 refs.)

Laboratory of Chemical Pharmacology
National Heart Institute
NIH
Bethesda, Maryland

2917 Kapp, Frederic T., & Gottschalk, Louis A. Drug therapy. Progress in Neurology and Psychiatry, 1962, 17, 536-558.

Major tranquilizers, minor tranquilizers, antidepressants and psychomotor stimulants are detailed. Side effects and complications of major tranquilizers are given. The evaluation of drugs for use in psychiatry is difficult and complicated. Preclinical data on animals is often of little value in predicting the outcome of therapeutic trials in man. Drug trials in hospitals are often made on persons badly defeated in life, suffering rejection with no prospect of rehabilitation into their former culture, while on the other hand most outpatients have a world about them

with which they are interacting. These great differences between in and outpatients make a carryover of information of 1 type to the other difficult and uncertain. Placebo effect is amplified. The control of abnormal behavior and the lessening of symptoms by major tranquilizers is not great enough; better answers about mental illness will be found when psychopharmacology considers man in all his relationships. (290 refs.)

[No address]

2918 Ulett, George A., Smith, Kathleen, & Bidy, Ralph. Shock treatment. Progress in Neurology and Psychiatry, 1962, 17, 559-571.

Techniques of ECT, complications, selection of patients and mode of action are reviewed. Tranquilizers appear to be about equally effective to ECT in most cases of manic and schizophrenic reactions. Reserpine combined with ECT is contraindicated, but the combination of ECT with the phenothiazines appears safe, except with massive doses. No conclusive statement can be made on the value of antidepressants versus ECT, however the combination of ECT with antidepressant is apparently safe. It does not appear that any of the antidepressants available can wholly replace ECT in the treatment of the more severe hospitalized depressions. There is as well a 3-21 day delay in antidepressant treatment allowing a period of time in which suicide may occur. (196 refs.)

[No address]

2922 Baker, Walter W. Pharmacology of the central nervous system. Progress in Neurology and Psychology, 1962, 17, 101-127.

Chlorpromazine and the phenothiazine derivatives, reserpine and related alkaloids, miscellaneous tranquilizing agents, depressants and analeptics, CNS stimulants, imipramine, MAO inhibitors, convulsants, cholinergics, catecholamines and 5HT, GABA, psychotomimetics, analgesic and anesthetic agents and anticonvulsants are reviewed. As well, drugs used in hyperkinetic disorders, antiparkinsonian drugs, muscle relaxants and neuromuscular blockers are outlined. (279 refs.)

[No address]

2923 Kline, Nathan S. Drugs are the greatest practical advance in the history of psychiatry. *New Medical Materia*, 1962, 4, 49.

Hospital discharges resulting in lower numbers of patients are largely due to the introduction of psychopharmaka since 1956. A projected 60,000 patient increase for the past 5 years has not materialized and there are about 23,000 fewer patients in mental hospitals than there were in 1956. In New York State alone, where drugs have been widely used, the decrease since 1955 has been more than 7,000 patients. As an indication of ward behavior, in Rockland State Hospital in 1955, 8,000 window panes were broken, while in 1960 only a mere 1,900 windows were broken. (No refs.)

Rockland State Hospital
Orangeburg, New York

2924 Natoli, A. Sulla terapia con tranquillanti e sedativi nei vecchi. [On therapy with tranquilizers and sedatives in the aged] *Progresso Medico*, 1962, 18, 506-507.

With the increase in the population of the aged, tranquilizers and sedatives are used increasingly in the control of insomnia, psychomotor agitation, anxiety, behavior disturbances and confusional states. The drop in popularity of reserpine and the rise of phenothiazine derivatives are cited, and daily doses advised for these drugs. Contraindications for bromides are cited. The efficacy of various tranquilizers, antidepressants and sedatives are briefly outlined. (3 refs.)

[No address]

2925 Napolitano, L. Sull'impiego dei tranquillanti in psichiatria. [On the use of tranquilizers in psychiatry.] *Progresso Medico*, 1962, 18, 117-118.

The general role of tranquilizers in medicine is discussed. The direct conflict between the fundamental principles of psychoanalysis and the administration of tranquilizers is noted. The International Symposium on Psychotropic Drugs held at Milan, May 1957 is cited. (4 refs.)

[No address]

2926 Shore, Parkhurst A. Release of serotonin and catecholamines by drugs. *Pharmacological Reviews*, 1962, 14, 531-550.

The following topics are discussed: agents releasing both serotonin and catecholamines (reserpine, benzoquinolizines, decarboxylase inhibitors and related agents and other agents), procedures modifying the ability of agents to release amines (MAO inhibitors, chlorpromazine and stress), agents affecting mainly catecholamines in peripheral tissues (guanethidine and related compounds and tyramine and other noncatechol sympathomimetic amines), and agents which block the uptake of catecholamines by peripheral tissues. (111 refs.)

Department of Pharmacology
University of Texas Southwestern Medical
School
Dallas, Texas

2927 Delgado, Jaime N. & Worrell, Lee F. Drug Notes, Psychopharmacologic, antidiabetic agents; anabolic steroid reviewed. *Texas State Journal of Medicine*, 1962, 58, 431-432.

Chlorprothixene (Taractan) leads to tranquilization without depression and may be therefore used in cases of agitated depression. It is better tolerated than the phenothiazines and favored for outpatient use. It is indicated in moderate to severe emotional disorders, especially agitated states. It is reported relatively free from severe toxic effects. (No refs.)

College of Pharmacy
University of Texas
Austin, Texas

2928 Texas State Journal of Medicine. Upjohn withdraws Monase from market. *Texas State Journal of Medicine*, 1962, 58, 372. [Editorial]

The Upjohn Company has announced the withdrawal of its product etryptamine (Monase) from the market because of the occasional development of agranulocytosis. It was 1st marketed in June 1961 and used in the

treatment of depression. (No refs.)

Texas Medical Association
1801 N. Lamar Blvd.
Austin, Texas

2929 Killam, Eva King. Drug action on the brain-stem reticular formation. *Pharmacological Reviews*, 1962, 14, 175-223.

Major topics reviewed are: fundamental considerations of structure and function of the brainstem reticular formation (anatomical investigations, afferent connections, special neural aggregations for autonomic integration and efferent connections--the functional role of the reticular formation in CNS regulation), methodological considerations in drug research, the influence of drugs on the reticular formation (chemical mediators, sedative-anesthetic agents, phenothiazines and Rauwolfia alkaloids, miscellaneous sedatives, muscle relaxants, stimulants, psychotomimetics and miscellaneous centrally active compounds (opioids, anti-convulsants, antiparkinsonian agents). (14 refs.)

Department of Pharmacology
Stanford University School of Medicine
Palo Alto, California

2930 Silvette, H., Hoff, E. C., Larson, P. S., & Haag, H. B. The actions of nicotine on central nervous system functions. *Pharmacological Reviews*, 1962, 14, 137-173.

The effects of nicotine on spontaneous activity, CR's learning, higher cerebral functions (sensorimotor functions, brain potentials, tremor, convulsions, nicotine paralysis and catelepsy), medullary functions (vomiting, respiration and vasomotor functions), cerebellar functions and spinal functions are reviewed. (184 refs.)

Departments of Pharmacology and Neurological Science
Medical College of Virginia
Richmond, Va.

2931 Weiss, Bernard, & Laties, Victor G. Enhancement of human performance by caffeine and the amphetamines. *Pharmacological Re-*

views, 1962, 14, 1-36.

Laboratory, military field and athletic performances on caffeine and amphetamine in relation to physical endurance and capacity, motor coordination and control (reaction time, steadiness and coordination), monitoring, learning, simple and complex verbal and arithmetic tasks, and effects on judgment and mood are reviewed. (112 refs.)

Department of Pharmacology and
Experimental Therapeutics
The Johns Hopkins University School of
Medicine
Baltimore, Maryland

2932 Friedman, Arnold P. Treatment of chronic headache. *International Journal of Neurology*, 1962, 3, 338-397.

Vascular headaches of the migraine type, muscular contraction headache, headache of vasomotor reaction, non-migraine vascular headache and chronic posttraumatic headache drug therapy elucidated. In the late states of migraine, analgesics and sedatives are sometimes helpful. Migraine patients may profit to a limited extent from the prophylactic use of tranquilizers. Methysergide has proven effective. The most practical and useful nonnarcotic analgesic available still remains acetylsalicylic acid. Tranquilizers and muscle relaxants are recommended in the preventive treatment of muscle contraction headache. It must be emphasized however that drugs cannot replace insight and understanding of one's emotional problems. (9 refs.)

Department of Neurology
College of Physicians and Surgeons
Columbia University
New York, New York

2933 Canadian Medical Association Journal. Medicine and therapeutics. *Canadian Medical Association Journal*, 1962, 87, 1035-1036. [Editorial]

In a general meeting on medicine and therapeutics, Lindsay discussed drug therapy in anxiety and depression outlining the history of development of psychoactive drugs, proper clinical evaluation and need for double-blind

controls and study over a prolonged period of time for adequate evaluation. Hatfield discussed the dangers of drug therapy, mentioned thalidomide, toxic reaction to placebos, etc. (No refs.)

150 St. George Street
Toronto, Ontario
Canada

2934 Spaulding, W. B. Dangers in the use of some potent drugs. Canadian Medical Association Journal, 1962, 87, 1275-1281.

The hazards of antibiotics and thiazide diuretics are reviewed and the following information presented. Reserpine can increase gastric acidity, induce mental depression, and when used with digitalis leads to ventricular premature beats. Hazards of phenothiazines include jaundice, parkinsonism and tremors, convulsions, hypotension, and blood dyscrasias. The butanediols have numerous side effects including gastrointestinal, cutaneous and hypotensive reactions. (48 refs.)

Department of Medicine
University of Toronto
Toronto, Ontario
Canada

2935 Canadian Medical Association Journal. Drugs and congenital malformations. Canadian Medical Association Journal, 1962, 87, 1288-1290. [Editorial]

Note is made of the 17 Nov., 1963 British Medical Journal report where a woman had taken 25 mg. of phenmetrazine t.i.d. in early pregnancy and given birth to an abnormal infant. Distressing reports in the Canadian Press are noted, and the fact depreciated that the Italian Government withdrew the drug from the market on the basis of this report. Approximately 500,000 pregnant women have used the drug in a 6-year period in North America since it was placed on the market in 1956. Similar reports incriminating meclozine, trifluoperazine, etc., with insufficient evidence of any teratogenicity, are cited. (12 refs.)

150 St. George Street
Toronto, Ontario
Canada

2936 Hastings, Donald W. Depression. Journal Lancet, 1962, 82, 9-11.

In a discussion of evaluation, physicians' attitude, family attitudes and therapy in depression, ECT, is cited as the backbone of treatment. Reports in the literature appear conflicting in relation to the value of antidepressants. With suitable outpatients, usually the physician preferred 1 or another of these drugs and gives it a therapeutic trial for a minimum of 2 weeks. If there is little or no change for the better after 2 weeks "try one of the others." (No refs.)

Department of Psychiatry
University of Minnesota
Minneapolis, Minnesota

2937 Journal of Iowa Medical Society. Sadove says addicts shouldn't be regarded as criminals. Journal of Iowa Medical Society, 1962, 52, 38. [Editorial]

Max S. Sadove deplores the practice of regarding drug addicts as criminals when they are really peaceful, nonbelligerent individuals (except when in need of a fix). In Great Britain addicts can register at a regional clinic and receive a plethora of legally prescribed drugs. Americans should emulate this example and provide narcotics (by controlled prescription, of course) for those so addicted. These unfortunate derelicts should also be regarded as human beings who desperately require our understanding. (No refs.)

Iowa State Medical Society
529 36th St.
Des Moines 12, Iowa

2938 Journal of Iowa Medical Society. Drug treatment for mental patients. Journal of Iowa Medical Society, 1962, 52, 48. [Editorial]

A film short entitled "No Man Is a Stranger" (Audio-Visual Department, Schering Corp., 1011 Morris Avenue, Union, N. J.) deals with the history and treatment of mental disorders in Haiti. Minimal hospitalization and maximal reliance on drug therapy are emphasized. Patients receiving main-

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tenance therapy are soon able to resume productive activity. (No refs.)

Iowa State Medical Society
529 36th Street
Des Moines 12, Iowa

2939 Chemotherapy. Progress in imipramine therapy. Depressive states, combination therapy. Chemotherapy, 1962, 2, 183-184. [Editorial]

Imipramine has proven to be efficacious in ameliorating depressive states according to Blair, Kiloh and Ball's double-blind studies. Succinct resumes of all work provide relevant information as regards dosage, duration, results and side effects. (3 refs.)

[No address]

2940 Chemotherapy. Amitriptyline: a new tranquilizer and antidepressive. Chemotherapy, 1962, 2, 182. [Abstract]

A review of amitriptyline cites work by Freed, Dorfman, Barsa and Saunders to emphasize the fact depressed patients respond dramatically to amitriptyline therapy with only minimal side effects. Salient facts are presented from several studies. (No refs.)

[No address]

2941 Kris, Else B. Post-hospital care of patients in their community. Current Therapeutic Research, 1962, 4, 200-205.

Tranquilizers like triflupromazine or fluphenazine, sometimes combined with antidepressants, are frequently used in maintenance therapy of released chronic patients. General procedures, pharmacotherapy, the day hospital, employment, and the patient and the community are discussed. (No refs.)

Department of Mental Hygiene
State of New York
New York, New York

2942 Canadian Medical Association Journal. Thalidomide embryopathy. Canadian Medical Association Journal, 1962, 87, 51 & 55.

Various reports from Germany relating to the thalidomide tragedy are reviewed, and incidental mention is made of acetylsalicylic acid (anemia), phenacetin (nephropathy). (No refs.)

150 St. George Street
Toronto, Ontario
Canada

2943 Canadian Medical Association Journal. Thalidomide embryopathy. Canadian Medical Association Journal, 1962, 87, 39-40. [Editorial]

The report of Lenz and Knapp (1962) in which retrospective histories of 122 mothers of malformed infants gave acceptable evidence of thalidomide intake during early pregnancy in 90 cases is discussed. Observations tend to show that the critical period for thalidomide is no longer than 14 days, but even during this period the main risk is probably concentrated in the 1st half; i.e., between the 27th and 33rd day after conception. (1 ref.)

150 St. George Street
Toronto, Ontario
Canada

2944 Theoret, John J. Chronology of the thalidomide story. Canadian Medical Association Journal, 1962, 87, 981-982.

The great care and diligence of Richardson Merrell scientists are propounded and the significant events in the history of the thalidomide tragedy are given, beginning with its synthesis by Chemie Gruenthal in 1953 through to the spring of 1962 when it was withdrawn from the market. (No refs.)

Wm. S. Merrell Company
Box 158
Weston, Ontario
Canada

2945 Stevenson, Lloyd G. Withdrawal of drugs. Canadian Medical Association Journal,

1962, 87, 1033.

McGill faculty members have expressed concern over the withdrawal from the Canadian market of certain chemical agents considered valuable in treatment. When new regulations are framed, it should be kept in mind that exploration be "carried only by persons well versed in this field and associated with recognized academic or research institutions (American Society for Pharmacology and Experimental Therapeutics 1962)," and a distinction should be made between drugs which are of their very nature dangerous and those (including almost all drugs of any potency) which can on occasion be dangerous if misused. (No refs.)

McGill University
Montreal, Quebec
Canada

2946 Minerva Farmaceutica. A psychotomimetic drug: *Coriaria thymifolia*. Minerva Farmaceutica, 1962, 11, 179. [Editorial]

The pharmacology of an extract from *Coriaria thymifolia* (member of the Coriariaceae from Ecuador), as reported by P. and E. Naranjo (Arch. Criminol. Neuropsiq., Quito, 1961, 9, 600), is outlined. In rats it has an action similar to that of lysergide and harmine, causing a transitory drop in blood pressure, stimulation of respiration at low doses and inhibition at high doses, also prolonged inhibition of intestinal contractility. It causes a variety of motor disturbances, including chronic convulsions. The LD 50 of the glucoside in mice is 96 mg/kg. (No refs.)

Edizioni Minerva Medica
Corso Bramante 83/85
Turin, Italy

2947 Himwich, H. E. Chapters 14, 23, 24 and 25. Progress in Neurology and Psychiatry, 1962, 17, 266-275; discussion 275-277.

After mention of LSD and BOL effects, the inadvisability (Williamina Himwich's clinical results) of combining imipramine (Tofranil) with MAO inhibitors is stressed. The patients exhibit profuse sweating, extreme restlessness and hyperexcitability, generalized convulsions and hyperpyrexia and 1 of

these patients died with a temperature of 109° F. It seems that any MAO inhibitor yields the same results: phenelzine (Nardil), nialamide (Niamid), tranlylcypromine (Parnate), iproniazid (Marsilid), isocarboxazid (Marplan), and a mixture of trifluoperazine and tranlylcypromine. All these MAO inhibitors produced untoward effects when given with imipramine. Brodie's hypothesis that 5HT may be the neutral transmitter in place of acetylcholine in the brain and the suggestion that levarterenol is active as a neurotransmitter is noted. Marazzi's views on 5HT blocking at the transcallosal synapse, as well as other information on neurotransmitters were elucidated in the discussion. (19 refs.)

[No address]

2948 Alonso Jimeno, S. Psicofarmacos. [Psychopharmaka.] Medicina, 1962, 30, 133-140.

The classification of psychoactive drugs, after Delay, is given in the scheme below:

Psycholeptics

Hypnotics or hypnosedatives

Barbiturates

Neuroleptics

Haloperidol

Chlorprothixene, etc.

Tranquilizers

Phenothiazine derivatives

Chlorpromazine

Mephenesin

Rauwolfia alkaloids

Captodiamine

Hydroxyzine

Chlordiazepoxide

Benactyzine

Meproamate

Psychoanaleptics

Psychotonics

Amphetamines

Centrophenoxine

Thymoleptics

Imipramine

MAO inhibitors

Psychodysleptics

Old

Alcohol

Marihuana

Ergot

Modern

Mescaline
LSD
Harmine, harmaline
5HT and epinephrine metabolites

[No address]

2949 Médecine et Hygiène. Psycholeptiques [Psycholeptics.] Médecine et Hygiène, 1962, No. 5402, 212-213.

This chart gives commercial names, chemical description, structure, mode of action, and CNS effects, as well as neurological and psychiatric indications, side effects, and particulars for the antidepressants nialamide, iproniazide, pizazide, phenelzine, tranylcypromine, imipramine, amitriptyline, phenpropionylamine, troxazine, and mephenoxalone. (No refs.)

[No address]

2950 Greene, Raymond. Thalidomide and congenital abnormalities. Lancet, No. 7253, 452.

Regardless of the thalidomide tragedy, it has often been demonstrated that animal experiments cannot obviate risk. Clinical testing of new drugs must continue and some risk must be expected or we must do without new drugs. (No refs.)

[No address]

2951 Cleghorn, R. A., Moll, A. E., & Roberts, C. A. [Eds.]. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1-746.

This volume of papers of the Third World Congress of Psychiatry held in Montreal, 4-10 June, 1961 contains papers ranging through the entire gamut of psychiatry. Child and family psychiatry, concepts and methods, mental hospitals, neurophysiology, physical therapy, psychopathology, psychotherapy, social psychiatry, aftercare, communication, community mental health, alcohol and drug dependency, electroencephalography, genetics,

group psychotherapy, juvenile delinquency, neuropsychiatry, organic psychoses, biochemistry, geriatrics, hypnosis, personality development and other topics are expounded. (1293 refs.)

University of Toronto Press
Toronto, Ontario
Canada

2952 Cleghorn, R. A., Moll, A. E. & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 747-1420.

This volume is a continuation of papers of the Third World Congress of Psychiatry. Topics covered include psychiatric hospitals, psychoanalysis, psychoendocrinology, psychopathology, the study of psychoactive drugs, psychophysiology, psychosomatics, psychotherapy, schizophrenia, social psychiatry, forensic psychiatry, physical therapies, social stress, the role of medical students, suicide and death, teaching transcultural (anthropologic) psychiatry, children, depression, and an author index for both volumes, volumes I and II. (2611 refs.)

University of Toronto Press
Toronto, Ontario
Canada

2953 Sawyer, Charles H. Some effects of sex hormones on brain function. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 118-120.

In discussions largely based on rabbit experimentations, brain sites and mechanisms of hormonal influence are reviewed. The basal hypothalamus is directly sensitive to sex steroids. By lowering or raising a reticular activating system, and hypothalamic EEG arousal threshold the steroid activates or inhibits, respectively, estrous behavior. By its similar action on a rhinencephalic and hypothalamic EEG after-action threshold, the steroid increases or decreases the facility with which the pituitary gland is activated to discharge pituitary gonadotropin. Ca-

capacity to elevate differentially the 2nd threshold categorizes the antifertility progestogens. There is evidence of threshold changes attributable to the direct feedback of released pituitary hormones. The appropriate interaction of hormones and brain function ensures coordination of sexual behavior and pituitary-gonad activity for successful reproduction and maintenance of species. (17 refs.)

University of California
Los Angeles, California
31

2954 Reiss, Max. Endocrine research in psychiatry. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 121-127.

The influence of hormones and the biochemical concomitance of their action on brain function is reviewed, especially in relation to disturbances in the quantity and quality of internal secretion. In attempts to correlate mental and physical states, much effort and disappointment could be saved if more patients were more carefully investigated from the physical point of view. Hormones should be given only with sufficient indications and even then the result is highly problematic unless their action is properly controlled. (10 refs.)

Willowbrook State School
Staten Island 14, New York

2955 Caffey, Eugene M., Jr. Controlled studies of tranquilizing and antidepressant drugs in 2,000 hospital patients. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 149-151.

The Cooperative Program of Research in Chemotherapy conducted by the VA is detailed. The VA operates 170 hospitals where 90% of the beds (58,414) are set aside for psychiatric cases. In 1956 the program of cooperative evaluation of psychotropic drugs was inaug-

urated. In studies on phenothiazines in the treatment of schizophrenics there is still doubt as to whether results are due to pharmacological action alone, to a patient-pharmacology interaction or to a patient-pharmacology-milieu interaction. Further there is a real problem in distinguishing side effects from psychiatric symptoms, e.g., insomnia. More should be learned about the role of psychoactive agents in the treatment of the elderly, about the length of time the drug should be administered and about combinations of chemotherapy with other major treatment methods such as psychotherapy. (12 refs.)

VA Hospital
Perry Point, Maryland

2956 Lopez-Ibor, J. El sintoma "clave" en el tratamiento de las depresiones. [The key symptom in the treatment of depression.] In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 165-169.

The efficacy of a drug can be assessed by observing its capacity to reduce, alter or eliminate target symptoms (behavioral, somatic, and experiential symptoms). In endogenous depression, the central symptom is vital sadness, which is an expression of alteration in vitality. The rate of remission with imipramine obtained in Spain is about 69%. (No refs.)

[No address]

2957 Lewis, Nolan D., Tobin, Joseph M., Boyle, Daniel, & Caton, John. Psychopharmacological research in an outpatient setting. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 374-379.

Parameters involved in multi-physician double-blind crossover psychopharmacologic research in an outpatient setting are detailed. The patient's attitude towards participation in such a study appears to be the most challenging area of investigation and suggests the need for the development

of test techniques more refined than those used to date. For example, drug reactors will respond differently to the same agent or similar agents at different points of time. The comparison of new with standard drugs is preferred if the pharmacological profile of the agent is comparable. While side effects have not generally been a major cause for drug discontinuation, behavioral toxicity, i.e., the patient's acting out of aggressive impulses, has occasionally presented problems. A double-blind study of 4 drugs (chlordiazepoxide, meprobamate, perphenazine and thioridazine) is detailed with an emphasis on variables. (16 refs.)

Bureau of Research in Neurology and
Psychiatry
Princeton, N. J.

2958 Fort, Joel. The use and abuse of alcohol and narcotics around the world. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 398-401.

Ten percent of the French population of 45 million suffers from alcoholism. This means that 1 out of every 4 or 5 adult men plus a considerably smaller number of women are alcoholics. Normal consumption is up to 4-5 liters/day for the average male. Cirrhosis and secondary psychiatric problems are the main consequences with accidents and drunken driving running close behind. Twenty-five percent of male and 10% of female admissions to state hospitals have alcoholic psychosis, a total of 30,000 admissions per year. Treatment programs involve vitamins, disulfiram, tranquilizers, and sometimes psychotherapy. In contrast France has an almost negligible narcotic addiction problem, about 1,000 individuals. However France is involved in the narcotics traffic of heroin from Lebanon for dissemination to Italy and the United States. Alcoholism in the United States is second only to France, i.e., 3% or 5 million alcoholics. The loss per year in accidents, absenteeism and job loss is approximately \$1 billion. Narcotics addiction is a far smaller problem affecting 50-100 thousand Americans. Hong Kong has the highest known incidence of narcotics addiction, ca. 10% of its 4-4.5 billion Chinese using opium or

heroin. About 70 thousand narcotic addicts live in Thailand, population 21 million. The alcoholism incidence rate for Sweden, 7 million people is about 2%; there is also a beginning narcotic addiction problem. Alcohol is a problem of the Western World, while narcotics addiction is a problem of the East. Addiction reflects the poverty, hunger, racial and religious discrimination, nuclear conflict, corruption, lack of education, cynicism, apathy, monotony, boredom with one's job, greed, ignorance, and immaturity which plague mankind. (No refs.)

Center for Treatment and Education on
Alcoholism
Oakland, California

2959 Lucena, José. La symptomatologie du cannabisme. [The symptomology of cannabism.] In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 401-406.

Disturbances in affect, thought patterns, attention and memory, evaluation of space and time, psychomotility and emotional expression, volition, perception, and the occurrence of delirium, modifications of conscience and self concept related to the smoking of marihuana are detailed. (28 refs.)

Université de Recife
Recife, Brazil

2960 Ammar, S., & Barek, E.M. Study of the evolutive aspects of toxicophilia in Tunisia. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 407-412.

Social and legal considerations related to toxicomania in Tunisia are discussed. Under the French Protectorate, marihuana and its sale were legal and traffic in heroin was tolerated. Poverty, vagabondage, proselytism, and absence of healthful forms of recreation were at the root of the problem. Since independence (1956) and the proclamation of the Republic, far-reaching structural

reforms in Tunisia have entirely changed aspects of the problem. There is now a law against marihuana and heroin stockpiles were destroyed in 1956; cases of toxicomania have considerably decreased. However along with these positive results, alcoholism is apparently on the increase. (No refs.)

Tunis, Tunisia

2961 Takman, John. An epidemiological study on narcotic use among Stockholm adolescents: a preliminary report. In: Cleg-horn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 412-415.

A drug problem among Stockholm youth began in 1958. The earlier incidence rate of narcotic use in 1954 and previous years was 8 compared with: 4 in 1955, 4 in 1956, 4 in 1957, 17 in 1958, 11 in 1959, and 2 in 1960. Amphetamine, phenmetrazine, and morphine are noted. Towards the end of 1957, Preludin (phenmetrazine) was introduced into Sweden as a weight reducer. As a consequence, the dope market, formerly very limited, suddenly had a boom as dozens of unscrupulous persons sent fat girls to doctors for phenmetrazine prescriptions. Still the drug problem is a minor one in Sweden. (6 refs.)

Stockholm City Child Welfare Board
Stockholm, Sweden

2962 Lemere, Frederick. The use of drugs in the treatment of alcoholism. In: Cleg-horn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 415-417.

Acute intoxication may be treated with mild temporary sedation, tranquilizers, vitamins, liothyronine, i.v. fluids and gradual withdrawal of alcohol. Definitive therapy of chronic alcoholism may utilize emetine (to produce a CR aversion), disulfiram or citrated calcium carbamide, all designed to help the patient remain abstinent. As the alcoholic is addiction-prone, sedative and many of the tranquilizers including meprobamate

should be prescribed only in special situations. Phenothiazines such as chlorpromazine are an exception and may be prescribed without risk of excessive self-medication or addiction. The antidepressants such as MAO inhibitors are often helpful in those alcoholics who drink to relieve depression or its equivalents. These drugs are not habit forming but the amphetamines are and should be avoided in the treatment of alcoholism. (5 refs.)

University of Washington and Shadel
Hospital
Seattle, Washington

2963 Arlen, Harold W. The treatment and rehabilitation of drug addiction. In: Cleg-horn, R.A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 431-435.

Drug addict rehabilitation as practiced in California is detailed. The necessity of institutionalizing patients during the initial days of treatment for drug addiction to accomplish withdrawal from physiological dependence has achieved the status of a "sine qua non." The rehabilitation of the drug addict is essentially the same as the rehabilitation of any patient whose compromised ego strength has rendered him particularly vulnerable to the stresses of life. The 1959 Narcotic Treatment Control Project of the California Department of Correction is reviewed. (No refs.)

South California Parole Outpatient Clinic
Beverly Hills, California

2964 Hurst, Lewis A. Research implications of converging advances in psychiatric genetics and the pharmacology of psychotropic drugs. In: Cleg-horn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 538-542.

The comparison of the mechanisms of antidepressants shows that 2 types of antidepressants (MAO inhibitors and imipramine), despite

fundamental differences in chemical structure and numerous differences in their detailed chemical effects, nevertheless a similar influence on 5HT and catecholamines, strengthening the view that these are the significant chemical entities involved in the therapeutic action of both types of drugs. This comparison pinpoints the search for the etiological enzyme block postulated by genetic evidence on the field of 5HT, catecholamines and their progenitors. Enzyme chemistry, neurochemistry, and neuropsychopharmacology, including the advent of the psychotomimetic and psychotropic drugs are briefly noted. Psychiatric genetics and neuropsychopharmacology are brought to a more defined focus by consideration on the specificity of action for the depressive states vis-à-vis schizophrenia of the mentioned antidepressants and the similarity of clinical outcome in depression with either MAO inhibitors and imipramine. (11 refs.)

University of Witwatersrand
Johannesburg, South Africa

2965 Sankar, D. V. Siva, Gold, Eleanor, Phipps, Edward, & Sankar, D. Barbara. Biochemical studies on schizophrenic children. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 610-613.

The biochemistry of schizophrenic and autistic children is reviewed with emphasis on the excretion of total aromatic amines and total indole compounds. Absence of galactosemia in autistic children is noted. The study of 5HT uptake by platelets is altered not only in childhood schizophrenia but also in adults subsequent to the administration of tranlylcypromine and chlorpromazine. A 5HT analogue may be produced in schizophrenia which passes through the same metabolic sites as 5HT does. Thus it is possible that a study of 5HT level and uptake in platelets may throw more light on the biochemistry of schizophrenia. (19 refs.)

Creedmoor State Hospital
Jamaica, New York

2966 Batt, J. C. Review of endocrinological investigations at St. Ebba's hospital. In:

Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 824-829.

Nine-hundred and ninety-five mental patients were tested for thyroid function (i.v. injection of 29 μ c I¹³¹--1 st iodine uptake at the end of 1 hour, at the end of 24 hours and the amount excreted at 24 and 48 hours, and PBI), adrenal function (17-ketosteroids and total ketogenic corticoid output over 24 hours and creatinine). Roughly 1 patient in 4 had a pathological I¹³¹ uptake and 1 in 8 a pathological PBI. The figure of 25% is somewhat less than the approximately 33% of abnormalities of thyroid which were observed in schizophrenics. Abnormal 17-ketosteroid excretion occurred in about 37% and no less than 60.9% had an abnormal total ketogenic corticoid output comparing recovered and unrecovered cases; 17-ketosteroids were low in 32.6% before treatment and 26.5% after, a relatively small difference, but the abnormal total ketogenic corticoids fell from 60-8 to 7.8% after treatment. Thyroid figures were less impressive and creatinine output roughly followed other figures for adrenal function, though changes were less marked. Several cases demonstrating individual responses to tranquilizers and hormones are detailed. (4 refs.)

St. Ebba's Hospital
Epsom, Surrey
Great Britain

2967 Barahona Fernandes, H. J. Pharmacopsychothérapie. [Pharmacopsychotherapy.] In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 896-901.

Combined psychotherapy and drug therapy, with a strong reliance on drugs, is reviewed. For example, in the psychotherapy of anxiety, imipramine-chlordiazepoxide, used for 8-12 days, can allow the patient to see the tragic situation in a realistic and objective way, thereby providing access for analytic techniques. Psychoanalytic orientation is not applicable to the pharmacopsychotherapy

of depressions except, as a rule, in the convalescent stage. The doctor-patient relationship in regard to the prescription of drug is stressed. (No refs.)

[No address]

2968 Fontana, Alberto E. Clinical use of hallucinogenous drugs. In: Cleghorn, R.A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 942-944.

There is an evident advantage gained by the use of hallucinogenic drugs, chiefly LSD, as aids to psychotherapy via the achievement of greater coherence, insight, and a reduction in the length of treatment necessitated. The psychotherapeutic process is the same with or without such drugs, but with their use mechanisms become more evident, disclosing a pattern of connection with reality after a deep regression beyond limits accompanied by the continuous evoked movement of contact and isolation which is expressed in terms of transference relationship. It is a real process of individualization where the subject is reborn and comes to life striving to reconstruct the deformed relationship with internal and external objects. Group therapy indications are exactly the same as individual psychotherapy. These techniques have also been carried out with children of various ages and diagnoses. (No refs.)

[No address]

2969 Ostow, Mortimer. Psychoanalysis and psychiatric drug therapy. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 951-955.

Psychoactive drugs can be used to start psychotherapy with the schizophrenic patient, the manic, or melancholic, who is too sick to participate in the analytic procedure and therefore has traditionally been considered unsuitable for psychoanalysis. Melancholia can frequently be relieved within

weeks with the aid of one of the energizing drugs. Drugs do not combat disease directly but act to correct a disturbance of psychic function created by disease and offer only symptomatic therapy, i.e., no drug is currently available that can undo the dynamic disturbance in family relations that lies at the basis of every neurosis and nonorganic psychosis. However, when dynamic forces become sufficiently strong to cripple ego functions, they can be attenuated by pharmaceutical means. (18 refs.)

[No address]

2970 Feer Hans. Vergleich der klinischen eigenschaften von drei phenothiazin-ähnlichen substanzen. [Comparison of the clinical effects of three phenothiazine derivatives.] In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 964-966.

The chemistry of chlorpromazine, chlorprothixene, amitriptyline, and imipramine is described rather extensively. Therapeutic and side effects are discussed in very general terms. Chlorpromazine is considered the drug of choice for treatment of schizophrenic psychoses; the other drugs, especially chlorprothixene and amitriptyline have mainly antidepressive effects. (2 refs.)

Psychiatrische Universitätsklinik
Basel, Switzerland

2971 Berthier, Ch. Les neuroleptiques sédatifs en thérapeutique psychiatrique. [Sedative neuroleptics in psychiatric therapy.] In: Cleghorn, R. A., Moll, A.E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 973-976.

The pharmacology and indications for levomepromazine, cyamepromazine, alimemazine, thioridazine, chlorprothixene, prothipendyl and combinations are reviewed. (No refs.)

Domité Lyonnais de Recherches Thérapeutiques
en Psychiatrie
Bron, France

2972 Levy, Sol. A new approach to the treatment of depressive reactions. In: Cleghorn, R. A., Moll, A. E. & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1357-1361.

The roles of psychopharmaka, ECT and psychotherapy in depression are discussed. Generally pharmacology is aimed at certain target symptoms, while convulsive therapy attacks the depression per se. Psychotherapy in depression is a rather complex problem and includes difficulty in rapport, difficulty with potential suicidal dangers, and etc. Tranylcypromine is found reliable in the treatment of mild depressions not endangered by suicidal risks. Imipramine is a well-tried agent and chlordiazepoxide is of use in mild depressions of recent origin. The successful use of sedatives for the suppression of insomnia, including thalidomide, is noted. (10 refs.)

[No address]

2973 Medical World News. New boost for 'GP psychiatry.' Medical World News, 1962, 3, 27. [Editorial]

Diazepam and chlordiazepoxide were reviewed in regard to clinical efficacy in anxiety and depression at the San Francisco Symposium on Neuropsychotropic Drugs. (No refs.)

Medical World Publishing Co, Inc.
30 Rockefeller Plaza W.
New York 20, New York

2974 Chemotherapy Review. Orphenadrine hydrochloride. Drug of choice in neuroleptic parkinsonism. Chemotherapy Review, 1962, 2, 139 & 155. [Editorial]

Success was obtained in alleviating neuroleptic parkinsonism with orphenadrine, which has also proved efficacious in ameliorating schizophrenic dejection and listlessness in conjunction with phenothiazines. Depressive states were also responsive to orphenadrine therapy. The combination of orphenadrine and thiopropazine is considered as being superior to ECT. (No refs.)

[No address]

2975 Chemotherapy Review. Chlorpromazine, schizophrenia and general hospitals. Chemotherapy Review, 1962, 2, 177. [Editorial]

Between 1950-1959, 95 schizophrenics, median age 32 years, were treated at St. Thomas' Hospital, London, by means of chlorpromazine, ECT, and modified insulin therapy. Of these, 42 were followed up as outpatients, 26 were seen at home and 6 were hospitalized. Overall, 86% were no longer hospitalized, 75% were largely cured, 26% still showed residual symptoms and 41% had relapses. Imipramine and phenelzine were utilized to combat depressive components as indicated. (1 ref.)

[No address]

2976 Grantham, Harry, Martin, Charles A., & Rouleau, Yves. Syndromes psychiatriques consécutifs à l'emploi des amphétamines. [Psychiatric syndromes following the use of amphetamines.] Laval Médical, 1962, 33, 85-89.

From 1956-1960, 11, 032 persons were admitted to clinique Roy-Rousseau (Quebec). Of these, 2,501 were admitted because of alcoholic intoxication and 164 because of intoxication due to drugs. With alcohol the figures were 2,245 men and 256 women, while with drug intoxication there were 58 admissions of men compared with 106 women. Twenty-four out of the 164 cases of drug intoxication were to amphetamines, 21 women and 3 men. (4 refs.)

Service de Femmes
clinique Roy-Rousseau
Université Laval
Quebec City, Quebec
Canada

2977 Aliaga, P., Escobar, M., Mejía, J., & Vargas, J. Ensayo con el bicorhidrato de tiopropazato en las psicosis crónicas. [Trial with thiopropazate in chronic psychoses.] Revista de Neuro-Psiquiatría, 1962, 25, 188-189. [Abstract]

Fourteen schizophrenics and 1 psychopath

(Archivos de Criminología Neuro-Psiquiatría y Disciplinas Conexas 1961) were treated with thiopropazate. Partial remission was obtained in 13%, social remission in 60% and failure in 25%. (1 ref.)

[No address]

2978 Solé Sagarra, J. Psicosis maniaco-depresivas. [Manic depressive psychosis.] Revista de Psiquiatría y Psicología Médica, 1962, 5, 644-666.

This is an abbreviated version of a work by the same name appearing in Tratado de Psiquiatría under the auspices of the Catedra de Psiquiatría de Barcelona, couched along the lines of Kleist (1959), following Kraepelin's (1918) system. In relation to treatment, ECT is preferred to pentetrazole shock. The usefulness of psychoactive drugs is stressed, especially imipramine. Promazine, methazine, perizine, and others including haloperidol, neuroleptics, MAO inhibitors, and tranquilizers are also useful in the treatment of endogenous psychosis. Neuroleptics are frequently of use in manic states. (46 refs.)

Instituto Pedro Mata de Reus
Neuropsiquiatra
Hospital Clínico de Barcelona
Barcelona, Spain

2979 Von Planta, Peter. Sur l'emploi clinique des inhibiteurs de la monoamine-oxydase dans l'angine de poitrine. [The clinical use of MAO inhibitors in angina pectoris.] Médecine et Hygiène, 1962, No. 541, 223-225.

Iproniazid, pheniprazine, isocarboxazid, phenelzine, nialamide and pivazid are discussed in relation to ambulatory patients with angina pectoris, particularly those with a neurotic, anxious, or depressive component. The psychostimulant and analgesic effect, dilatation of coronary arteries, diminution of oxygen consumption, accumulation of lactic acid, antithrombotic effect and the prevention of myocardial necrosis are reviewed. The most important side effects are lowering of blood pressure, most often orthostatic, hepatotoxicity, the possibility of cardiac insufficiency, and

the possible appearance of psychomotor excitation and manic states. (No refs.)

Laboratory Hoffmann La Roche
Basel, Switzerland

2980 Giberti, F. Problemi metodologica ed aspetti teorico-pratticidella moderna psicofarmacologia. [Methodological problems and theoretic-practical aspects of modern psychopharmacology.] Sistema Nervosa, 1962, 14, 437-453.

The classification of psychotropic drugs, general trends, ethics and methods of study and evaluation in clinical research, including the placebo problem and the question of quantitation in psychopharmacology are discussed (79 refs.)

Clinica delle Malattie Nervose e Mentali
Università Genova
Genoa, Italy

2931 Kolb, Lawrence. Drug addiction: A medical problem. Springfield: Charles C Thomas, 1962, Pp. 1-183.

The purpose of this book is to point out understanding of the addiction phenomenon and the development of programs of control and treatment which are compatible with the interest of the whole society. The chapter titles are: a perspective on drug addiction; drug addiction and crime; types and characteristics of cases of medically induced addiction; juvenile addiction; the struggle for cure and conscious reasons for relapse; pleasure and deterioration from narcotic addiction; effects of addiction of health; treatment of narcotic addiction; highlights in the history of addiction; propaganda about addiction, its cause, nature and effect and solution of addiction problem. (129 refs.)

NIMH
Bethesda, Maryland

2932 Welsh, Ashton L. Side effects of anti-obesity drugs. Springfield: Charles C Thomas, 1962, Pp. 1-243.

Obesity and its problems are reviewed. Side

effects and the role of central stimulating appetite distractors, i.e., amphetamine, methamphetamine, phenylpropanolamine, phenmetrazine, phentermine, and diethylpropion, are detailed. Sedatives and tranquilizers, bulk producers, dietaries and thyroxine, and sodium liothyronine are discussed at length. Management of a patient's obesity problem should include accurate diagnosis, psychological directions, recommendation of a balance, low-calorie diet, selection and prescription of accepted medications, and supervision of the weight-reducing program. (301 refs.)

University of Cincinnati
College of Medicine
Cincinnati, Ohio

2983 Hoffer, A. Niacin therapy in psychiatry. Springfield: Charles C Thomas, 1962, Pp. 1-165.

Information on the role of nicotinic acid therapy, especially in inhibiting senile mental changes and in reversing some of the changes produced by lysergide and adrenolutin are reviewed. Sixty case histories are included in the appendix. Nicotinic acid as a vitamin, its toxicity, nicotinic acid and nicotinamide as sedatives, their use in the treatment of schizophrenia and in confusion-al and drug-induced psychoses are detailed. A double-blind trial is described including 82 patients of various diagnoses treated 33 days with nicotinic acid or placebo. They were given the Weyburn Assessment Scale before and at various periods after treatment. Nicotinic acid or nicotinamide as 3 g/day or more, materially improved the recovery rate. Patients who were discharged as improved tended to remain better and had fewer remissions if they continued taking nicotinic acid or its amide. (122 refs.)

Psychiatric Services Branch
Department of Public Health
Saskatoon, Saskatchewan, Canada

2984 Kalow, Werner. Pharmacogenetics. Heredity and the response to drugs. Philadelphia: W. B. Saunders Co., 1962, Pp. 1-231.

This book discusses drug resistance in micro-organisms, drug responses of somatic cells in

tissue culture, resistance of insects, pharmacological effects and heredity in laboratory animals, heritable factors recognized in man by the use of drugs (e.g., prolonged action of succinylcholine and atypical cholinesterase, metabolism of isoniazid), human hereditary defects with altered drug response, including phenylketonuria and mongolism, and racial differences in the response to drugs. (1139 refs.)

Department of Pharmacology
University of Toronto
Toronto, Canada

2985 Stévenin, Laurent, & Benoit, J. C. L'utilisation des médicaments psychotropes en psychothérapie. [The use of psychoactive drugs in psychotherapy.] *Encéphale*, 1962, 51, 420-459.

Narcoanalysis, the use of pentothal in psychotherapy, is outlined, i.e., the hypnoid state. The use of 10-30 mg amphetamine i.v. to bring on emotional mobility and crisis in analysis is noted. Also the use of mescaline and LSD, and psilocybin is outlined. Further, the psychotherapy of patients treated with psychotropic drugs is discussed at length. (153 refs.)

Clinique de Maladies Mentales
1, rue Cabanis
Paris XIV, France

2986 Roessler, Robert & Greenfield, Norman S. [Eds.] Physiological correlates of psychological disorder. Madison: University of Wisconsin Press, 1962, Pp. 1-281.

Major trends in 20th century research; biochemical mechanisms in schizophrenia; psychophysiological methodology for the study of schizophrenia; excitability of the cerebral cortex in psychiatric disorder; consciousness in schizophrenia as a function of the peripheral microcirculation; some problems in psychophysiological research; some psychological factors related to cardiovascular responses: a logical and empirical analysis; control and artifact in psychophysiological research; hormonal activity and individual responses to stresses and easements in everyday living; adrenocortical function during anxiety, the role of defense in psychological

stress research on a disease: strategies in the study of obesity; some research on psychophysiological specificity and its relation to psychosomatic disease; psychosocial and psychophysiological studies of tuberculosis, and the incidence of somatic disease in psychiatric patients are discussed. Several aspects of the role of defense in psychological stress response are explored. These papers were given at the University of Wisconsin Medical Center, August, 1961. (484 refs.)

[No address]

2987 Arnold, O. H., St. Hift, & Hoff, H. The role of psychotropic drugs in current psychiatric therapy. *Comprehensive Psychiatry*, 1962, 3, 330-342.

Clinically 5 groups of psychopharmaka are differentiated: neuroleptics, tranquilizers, antidepressants, stimulants, and phantastica. The therapeutic application of neuroleptics applies to schizophrenia, manic-depressive reactions, organic confusional states, drug addiction, and neurotic states. The doctor must know when to administer tranquilizers, the "aspirin of psychiatry." An obvious abuse is an energizer on arising, and antidepressive when annoyed, a tranquilizer when restless and a hypnotic when sleepless. The use of imipramine and iproniazide, ECT, psychotherapy and guidance in depression is outlined, as is the induction of confusional states of the exogenous origin by psychotomimetics. (35 refs.)

Psychiatrische-Neurologische Klinik
Universität Wien
Vienna, Austria

2988 Marrazzi, Amedeo, S., Hart, E. Ross, Rodrigues, Jose M., Gluckman, Melvyn I., & Horovitz, Zola P. Correlation of the cerebral biochemical and functional effects of monoamine oxidase inhibitor antidepressants. *Progress in Neurology and Psychiatry*, 1962, 4, 266-277.

The close correlation between chemical changes induced, especially the increase in situ 5HT, and function at cerebral synapses has confirmed and strengthened the cerebral

synaptic neurohumoral role contributed to 5HT (serotonin). Through intracarotid arterial injection in the anesthetized cat, the cerebral actions of iproniazid, isoniazide, and pheniprazine were studied. Influence on tranccallosally evoked cortical potentials was used as the index of synaptic transmission, accomplished by denervation of the carotid sinus and by-passing the lesion. Cerebral concentration of MAO inhibitors, MAO activity, 5HT concentration and the ability of cerebral synapsy to transmit test impulses were assayed. Results allow the following hypotheses: a) augmentation of the existing distortion of synaptic equilibrium in the direction of inhibition of extending inhibition to sites that result in release phenomena or secondary activation; b) counteraction of excessive excitation due to existing distorted cerebral synaptic neurohumoral equilibrium by the inhibitory action of the locally accumulated 5HT, and c) an action unrelated to the MAO inhibitory effects of these antidepressants. These 3 alternatives are not necessarily exclusive, since they may apply to 3 different forms of mental disturbance whose underlying mechanism is characterized in 1 case by excessive synaptic inhibition, in another by excessive synaptic excitation, and in a 3rd by some as yet unclear mechanism. (15 refs.)

VA Hospital
Pittsburgh, Pennsylvania

2989 Schaefer, H. *Anesthesie und Narkose in der Praxis (II)*. [The theory of anesthesia (II).] *Therapiewoche*, 1962, 24, 1053-1054.

Various theories are reviewed relating to the effects of narcotic agents on the cell membranes, on the CNS as seen in the EEG, and on rise and fall of blood pressure. It is postulated that anesthesia, in all probability, causes the suspension of function of a desynchronized, activating, reticulo-thalamo-cortical system. Anesthesia is also regarded a psychophysical occurrence which abolishes the characteristics of pain (analgothymia). At least some narcotics intensify the depth of anesthesia by effecting the lowering of blood pressure. (No refs.)

Physiologische Institut
Universität Heidelberg
Heidelberg, Germany

2990 Van Eck, C. R. Ritsema Die Behandlung chronischer Schmerzzustände in der ärztlichen. [The treatment of chronic pain in the medical practice.] Therapiewoche, 1962, 24, 1055-1057.

The need for extensive diagnostic investigations at the onset of treatment for pain is emphasized. Chronic painful conditions as rheumatism, arthritis, neuralgia, are different from the pains of the terminal cancer patient. The 1st group has to learn to live with pain; the complaints can be reduced with medication, diet, and good health habits. For the 2nd group, the necessity for evaluation of the environmental conditions is stressed. The author has not used morphine, or morphine derivatives, in the treatment of this type of condition for years. Acetylsalicylic acid is the preferred analgesic, and its efficacy is close to that of morphine, while the analgesic efficacy of a placebo is approximately 50%. The combination of acetylsalicylic acid, phenacetin, and codeine is highly recommended because it is one of the most effective combinations. In the case of existing addiction to hypnotic agents, incomplete withdrawal and intensive occupational therapy are recommended. The prescription of tranquilizers is contraindicated, except for occasional psychological crises, or during the last days of life. (14 refs.)

Institut für Anästhesiologie
Reichs-Universität
Groningen, The Netherlands

2991 Therapiewoche. Thrombosegefährdung durch Barbiturate. [Barbiturate effect on thrombosis.] Therapiewoche, 1962, 16, 692. [Editorial]

Poumailloux has pointed out that barbiturates are able to influence the long-term therapy with anticoagulants by raising the prothrombin level. The prothrombin level may be elevated to such a degree that it may, in turn, cause occurrence of thrombosis or embolism. The use of barbiturates during anticoagulant therapy should therefore be avoided; if unavoidable, the barbiturates should be administered regularly and the dosage of the anticoagulant increased, in order to counteract the prothrombin level.

If the barbiturates are withdrawn, the anticoagulant has to be reduced in order to avoid possible bleeding. One of the few sedatives which can be administered during anticoagulant therapy without increasing the prothrombin level is glutethimide. (No refs.)

[No address]

2992 Deysson, Guy, De l'auxine à la sérotonine; acquisitions récentes sur le rôle biologique de certains dérivés indoliques et leur intérêt en pharmacologie. [From auxins to serotonin; recent information on the biological role of certain indole derivatives, and their value in pharmacology.] Produits et Problèmes Pharmaceutiques, 1962, 17, 62-71.

Both auxins and 5HT (serotonin) are products of tryptophane metabolism and involve similar enzyme systems in both plants and animals. The tryptophane, tryptamine, indole acetic aldehyde, indole acetic acid system is explained and contrasted to the tryptophane, 5HTP, 5HT, 5HIAA, 5 hydroxyindole acetic system. Auxins have been discovered in animals (indole acetic acid in the urine, known since 1903) and 5HT in plants (Bowden, Brown and Batty 1954). The structures of bufotenin, psilocin and psilocybin are outlined. Neurostimulants and antidepressants are discussed, particularly centroproxene. (100 refs.)

Faculté de Pharmacie de Paris
Paris, France

2993 Maccloni, S., Alejandro. Intoxicaciones agudas; generalidades. [Acute poisoning; generalities.] Pediatría, 1962, 5, 466-485.

Acute poisonings constitute a major problem in emergency pediatrics not only because of relative frequency, but also because of threat of death. Aside from common poisonings, intoxication in Chile by ingestion of the seeds of *Datura stramonium*; the symptoms are: mydriasis, flushed face and psychomotor excitation, accompanied by fever, delirium with visual or auditory hallucinations, crises of terror or euphoric states, etc. Poisonings by barbiturates and opioids, as

well as ethyl alcohol and phenothiazine derivatives are noted. (16 refs.)

[No address]

2994 Médecine et Hygiène. Narcotiques en injection: danger! A propos de l'Estil. [Injectable narcotics: Danger! On Estil.] Médecine et Hygiène, 1962, No. 542, 262. [Editorial]

Estil, produced by the Dr. Rudolf Reiss Chemische Werke, Berlin, was taken off the market at the end of February 1962, after a 17-year-old man lost his fingers by amputation following gangrene and the death of a woman from renal insufficiency following Estil. The narcotic might have been the cause of death. (No refs.)

22, rue Michell-du-Crest
Geneva, Switzerland

2995 Sirbu, Aurelia, Simulescu, Eugenia, & Stolla, Nicolae. Cu privire la medicatia psihotropă. [On psychotropic drugs.] Viata Medicală, 1962, 9, 538-590.

The advent of psychotropic drugs in 1952 and Delay's classification are outlined. Chlorpromazine, reserpine, levomepromazine, imipramine, meprobamate and other drugs are reviewed. (27 refs.)

[No address]

2996 Médecine et Hygiène. Psycholeptiques VII et VIII. [Psycholeptiques VII and VIII.] Médecine et Hygiène, 1962, No. 536, 116-117.

Details relative to phenothiazine derivatives; i.e., commercial names, generic names, structure, CNS effects, neurologic indications, psychiatric indications, side effects and peculiarities are presented. (No refs.)

22, rue Michell-du-Crest
Geneva, Switzerland

2997 Médecine et Hygiène. Psycholeptiques IX. [Psycholeptiques IX.] Médecine et Hy-

giène, 1962, No. 537, 145.

Details relative to rauwolfia alkaloids, giving commercial names, generic names, structure, CNS effects, neurologic indications, psychiatric indications, side effects and peculiarities are presented. (No refs.)

22, rue Michell-du-Crest
Geneva, Switzerland

2998 Medical World News. Sedative stirs up a new storm. Medical World News, 1962, 26-27, [Editorial]

New means must be found for avoiding the possibility of a tragedy in the future. Present drug testing procedures could not have predicted thalidomide's teratogenic effects. Duttmacher (Planned Parenthood Federation of America) stated that U.S. abortion laws make no provision for the child. There is no legal sanction for therapeutic abortion, but even in the absence of legal precedent, therapeutic abortions are being carried out in many U.S. Hospitals, possibly 75% of non-Catholic hospitals and 40% of Catholic hospitals. Laws have not kept up with medicine. (No refs.)

[No address]

2999 Medical World News. Drug safety rules proposed: thalidomide issue. Medical World News, 1962, 3, 22-23. [Editorial]

Proposed FDA rules would require manufacturers to supply the government with a detailed summary of all preclinical tests including animal studies, and prove that "it is reasonably safe" to begin clinical trials. If in a trial a "substantial doubt" about safety develops, a pharmaceutical house must stop the trial, notify FDA and recall all drug stocks. FDA itself can ban or halt clinical trials. (No refs.)

[No address]

3000 Guyotat, J. Association de la pharmacothérapie à la psychothérapie dans le traitement de névroses. [Combination of pharmacotherapy and psychotherapy in the

treatment of neuroses.] *Medicina Experimentalis*, 1962, 7, 87-99.

The function of neuroleptics is to break through a circle of stereotyped attitudes to the psychiatrist or to overcome the effects of an acute attack. Psychoanaleptics like imipramine or MAO inhibitors can aid in externalizing the patient's self-aggression into aggressive attitudes vis-à-vis the psychiatrist. Psycholeptics will frequently reinforce a long-standing attitude of despair, in which case MAO inhibitors will aid in attaining a breakthrough. Neuroleptics can also aid in the application of analytic techniques employed in teaching the patient to face reality. Working hypotheses are needed in order that (e.g. suppression of agitation by thioproperazine) may be more effectively employed for therapeutic ends. Neurotic depressions are treated primarily by imipramine-meproamate-chlorpromazine combinations. (No refs.)

Hopitaux Psychiatriques
Université de Lyon
Lyon, France

3001 Pogády, J., & Grígelová, M. Systém otvorených dverí v psychiatrickom ústav-níctve a ataraktika. [Open door policy in psychiatric institutions and ataractics.] *Ceskoslovenská Psychiatrie*, 1962, 58, 238-244.

Statistics are given from 1955-1961, with notes on the influence of psychiatric drugs, for the 160-bed female ward of the Regional Psychiatric Hospital of Pezinok. In 1955 the ward was closed. Classical shock treatment and an extensive occupational therapy program were in vogue. By 1958 while the ward was still closed, intensive occupational therapy and treatment with tranquilizers were current, shock treatment receding into the background. In 1960-1961 the open door system was introduced with concurrent rehabilitation on a wide scale and intensive psychopharmacotherapy. Study was made of verbal, physical and interpersonal aggression, the number of escapes, suicide attempts and suicides. The incidence of these parameters was lower in 1960 than in 1955. Verbal and physical aggression were considerably lower in 1960 compared to 1958. Verbal aggression

was more frequent in 1958 than in 1955. Differences in the relative frequency of attempted escapes and suicides through these years were not statistically significant. From the standpoint of safety and benefit to patients, the open door system could have been used at any time provided there was a consistent institutional regimen and occupational therapy. Ataractics are adjunctive in launching and maintaining an open door policy. Such a system has a favorable effect on normal interpersonal relations of both the patients and the staff. The role of psychotherapy in the elimination of morbid interpersonal relations and morbidity upon admission is stressed. (12 refs.)

Krajská Psychiatrická Liečebna
Pezinok, Czechoslovakia

3002 Ilavero, Francisco. Psicofármaco y personalidad (cuestiones de principio). [Psychopharmaka and personality: questions of principle.] *Médicamenta*, 1962, 14, 151-158.

Causes and motivations in psychosomatic medicine in relation to the specificity or non-specificity of psychoactive drugs are reviewed. The symptomatic nature of treatment with psychoactive compounds is stressed. In spite of the clinical efficacy of these drugs, they should not be abused, i.e., stresses of daily life are necessary to personality maturation. (12 refs.)

[No address]

3003 Journal of Iowa Medical Society. The hazards of amphetamine therapy. *Journal of Iowa Medical Society*, 1962, 52, 671. [Editorial]

Klich and Brandon (1962) studied amphetamine induced psychosis in 12 cases and the usage of amphetamines in Newcastle-on-Tyne, population 269,000. There, the equivalent of 200,000 5 mg tablets of amphetamine were being prescribed/month and evidence was uncovered that many patients were taking far more than the prescribed dosage. Habituation and addiction to the drug is common and abuse a problem of serious proportions. (1 ref.)

[No address]

3004 Journal of Iowa Medical Society. An organic theory of mental illness. Journal of Iowa Medical Society, 1962, 52, 133.[Editorial]

Fessel (1962) stated that there is a large body of evidence pointing to blood-protein abnormality in the mentally ill. These include an elevation of certain globulins and certain other protein substances. There is a significant elevation of the S-19 macroglobulins in persons with so-called functional acute mental disturbances, which macroglobulins imply an autoimmune factor in the genesis of some functional psychoses. (no refs.)

[No address]

3005 Journal of the American Pharmaceutical Association. The thalidomide story. Journal of the American Pharmaceutical Association, 1962, 2, 510 & 547. [Editorial]

Thalidomide was placed on the West German market in 1957 by Chemie Grünenthal, Stolberg, and the Wm. S. Merrell Co. licensed for investigation in the U.S. and Canada in January, 1959. In September 1961 Wiedemann reported the 1st series of thalidomide-deformed infants. Following suspicion of thalidomide voiced by Jenz, Grünenthal withdrew the drug from the market on November 26, 1961. A table of trade names and manufacturers containing drugs is provided. (1 ref.)

[No address]

3006 Castets, B., & Lefort, R. Les états dépressifs séniles. Etude clinique et thérapeutique. [Senile depressive states. Clinical and therapeutic studies.] Concours Médicale, 1962, 84, 4795-4798.

Senile depressive states involve progressive loss of interest in things and finally the development of neurologic disorders related to senile cerebral vascular changes. These alterations bring about temporal-spacial disorientation aphasia, sensomotor disorders, etc. Prophylaxis and home care are stressed. Hypotensive medications are to be avoided. Analeptics, vasodilators, anticoagulants, and rehydration are frequently indicated. (No refs.)

[No address]

3007 Kranzdorf, Charles D. Early recognition and management of depressions. California Clinician, 1962, 58, 237-239.

In view of the suicide factor the early recognition and management of depression are urgent matters. There are essentially 3 approaches: 1) psychotherapy, 2) chemotherapy and 3) shock therapy. Among available antidepressants, the phenylethylamines, MAO inhibitors and imipramine have had extensive clinical use. In view of rapid onset of action tranlylcypromine is recommended. The role of the general practitioner is stressed. (2 refs.)

Department of Psychosomatic Medicine
California College of Medicine
Los Angeles, California

3008 Cooper, Peter. Psycho-pharmacology: retrospect and prospect. Chemotherapy Review, 1962, 2, 164-167.

Reserpine and chlorpromazine 1st were used to alleviate mental illness 10 years ago. The advent of the phenothiazines represents the 1st great class of major antipsychotic drugs. Chlorpromazine has proved remarkably effective in manic psychoses, schizophrenia, senile agitation and anxiety. Phenothiazine derivatives display a marked propensity to provoke extrapyramidal reactions. Haloperidol appears far more effective than chlorpromazine. Other useful drugs include chlorprothixene, imipramine, and iproniazid, MAO inhibitors, isocarboxazid, phenelzine, etc. The milder tranquilizers include meprobamate and chlor-diazepoxide. Model psychoses may be induced with LSD, psilocybin and mescaline. (58 refs.)

[No address]

3009 Cameron, Dale C. Narcotic drug addiction. American Journal of Psychiatry, 1962, 119, 793-794.

With respect to narcotic addiction, the AMA and National Research Council support follow-up and rehabilitation procedures following complete drug withdrawal, compulsory civil commitment of drug addicts for treatment in a drug-free environment, augmentation of addict rehabilitation under continuing civil commitments, research on prevention and treat-

ment of addiction and dissemination of factual information on narcotic addiction. Treatment of drug addicts is a medical problem. Drug addiction in the US is a symptom of an underlying personality or emotional problem which precedes deleterious psychological, physiological and pathological changes. It is exceedingly difficult to achieve successful drug withdrawal in the absence of a drug-free environment. (No refs.)

[No address]

3010 Cooper, Peter. Drugs affecting the nervous system. *Chemotherapy Review*, 1962, 2, 100-102.

New psychoactive drugs include methohexital (an anesthetic), dichloralphenazone (a non-barbiturate sleeping preparation), phenmetrazine and amphetamine (for weight reduction), methylphenidate, vanillic acid diethylamide, trifluoperazine and thioridazine (thioridazine proved excellent for those who could not tolerate chlorpromazine), levomepromazine, Deprol (meprobamate and benactyzine), hydroxyzine, trimethobenzamide (an antiemetic) and triflupromazine (also used as an antiemetic). (No refs.)

[No address]

3011 Rassegna Internazionale. Novità per gli schizofrenici. [New information on schizophrenia.] *Rassegna Internazionale*, 1962, 42, 1336-1337. [Editorial]

The efficacy of haloperidol and triperidol in the treatment of schizophrenia is briefly noted. The former is useful in the reduction of agitation and aggressiveness; the latter improves catatonia, negativism and various states of indifference. (No refs.)

[No address]

3012 Pfeiffer, Carl C., & Smythies, John R. [Eds.] *International Review of Neurobiology*. Volume IV. London: Academic Press, Inc., 1962. Pp. 1-388.

This book covers the nature of spreading depression in neural networks; the organizational aspects of some subcortical motor areas; the biochemical and neurophysiological development of the brain in the prenatal period; substance P--a polypeptide of possibly physiological significance, especially within the nervous system; anticholinergic psychomimetic agents; benzoquinolizine derivatives--a new class of MAO decreasing drugs with psychotropic action, and the effect of adrenochrome and adrenolutin on animal behavior and human psychology. (854 refs.)

New Jersey Psychiatric Institute
Princeton, New Jersey

3013 Molhant, M. Le rôle et l'importance des nouveaux médicaments psychotropes dans le traitement des psycho-nevroses. [The role and importance of the new psychotropic drugs in the treatment of psychoneuroses.] *Presse Médicale*, 1962, 70, 377-379.

Psychotropic drugs fall into 2 major classes, psychosedatives including the tranquilizers: phenothiazine derivatives, rauwolfia alkaloids, thioxanthenes, butyrophenones and thiophenylpyridilamines, and the psychostimulants; including a) antidepressants, such as MAO inhibitors, imipramine, amitriptyline, etc., b) psychotonics e.g., amphetamine. A 3rd group includes the psychodyleptics (mescaline, atropine, lysergide, etc.). Their effects are purely symptomatic and their action is selective, varying from 1 person to another. No exact correlation can be established between dosage and clinical effects. They are polyvalent, with undesirable side effects at certain doses and liable to cause visceral complications. Psychodysleptics must be considered purely as adjuncts. (8 refs.)

[No address]

CLINICAL STUDIES

3014 Kagan, G. 'Librium' in anxiety and depressive states seen in general practice. *Chemotherapy Review*, 1962, 2, 231-232.

Eighty-one women and 29 men whose main complaint were anxiety and depression often associated with domestic difficulties were treated with chlordiazepoxide (Librium) for 4-6 weeks. The majority were given 20 mg chlordiazepoxide t.i.d. for the 1st week and if improvement was apparent, the dose was reduced to 10 mg t.i.d. Complete relief of symptoms was obtained in 62, marked improvement in 31, moderate improvement in 11 and little or no improvement in 5. Additionally about 15 children whose main complaint was bed wetting were treated with 5 mg b.i.d., many showing considerable improvement. A few patients complained of nausea, dizziness or drowsiness in the first few days of treatment.

Leek, Staffordshire
Great Britain

3015 Van Rhijn, C.H. An evaluation of means of a controlled group. *Psychiatria, Neurologia, Neurochirurgia*, 1962, 65, 117-128.

Fifty patients treated with thioridazine (Melleril) were observed for an average of 6 months: 22 chronic defective schizophrenics, 15 patients suffering from schizoid psychoses and 13 miscellaneous cases. Dosage ranged to 900 mg/day. Seventeen were markedly improved and 16 improved. Percentages of "good effect" on symptoms were: 50 paranoid, 33 delusory, 22 hallucinatory, 20 catatonic, 25 restless, 36 confused, 22 aggressive, 40 manic, 60 depressed and 50 anxious. Best results were obtained with patients with paranoid reactions. Catatonia reacted the least. Some slight drowsiness and paleness was noted.

Mental Hospital "Brinkgreven"
Deventer, The Netherlands

3016 Wells, B.G. The treatment of psychoneurotic patients with "Amylozine" (trifluoperazine/amylobarbitone). *Chemotherapy Review*, 1962, 2, 21-22.

Fifty-six anxiety depressive states were treated with from 2 to 6 capsules of Amylozine [(trifluoperazine and amobarbital) dosage unspecified] results were excellent in 42 cases, good in 6, fair in 2 and poor in 5. Side effects were few: heartburn was recorded in 1 patient and 2 patients who consumed small amounts of alcohol while on drug said that the effect of the drink was enormously increased. Alcohol should be forbidden to those on Amylozine until further experience is obtained.

[No address]

3017 Mossberg, Sanford M., Bloom, Alan, Berkowitz, Jesse, & Ross, George. Serum enzyme activities following morphine. A study of transaminase and alkaline phosphatase levels in normal persons and those with gallbladder disease. *Archives of Internal Medicine*, 1962, 108, 429-437.

Of 48 individuals with no known gallbladder disease, none exhibited an increase of SGOT or serum alkaline phosphatase activities following morphine administration. Significant morphine-induced SGOT elevations occurred in 5 of 6 cholecystectomized patients, in 1 of 2 with radiographically nonfunctioning gallbladders, and in none of 4 with demonstrable stones and radiographically functioning gallbladders. Serum alkaline phosphatase was concomitantly increased in 2 patients with cholecystectomy and in 1 with a nonfunctioning gallbladder. Transaminase increments were from 2 1/2 to 65 times control values while serum alkaline phosphatase increases did not exceed 3 times control values. Increased SGOT values must be viewed with caution in patients with combination of (a) suspected myocardial infarction, (b) normal or equivocal EGG, (c) biliary tract disease, and (d) prior narcotic administration. Biliary obstruction per se may provoke an elevation of SGOT and serum alkaline phosphatase activities. Functioning gallbladder acts as a safety-valve, reducing the effective intraductal pressure following biliary obstruction.

Department of Medicine
Montefiore Hospital
New York, N.Y.

3018 Hankoff, Leon D., Rudorfer, Leon, & Paley, Herbert M. A reference study of ataraxics. A two-week double blind outpatient evaluation. *Journal of New Drugs*, 1962, 3, 173-178. [No address]

The capsules, given t.i.d., contained 200 mg meprobamate, 50 mg chlorpromazine, 10 mg chlordiazepoxide or placebo. One-hundred-and-thirty-four outpatients treated were divided into 2 groups: schizophrenic and nonschizophrenic. The chief criterion was manifest anxiety, as measured by a 4 point scale. The Affect Adjective Check List was also used. In relation to untoward effects, chlorpromazine showed the highest incidences of reported somatic discomfort with 48%, in contrast to 29.6% with chlordiazepoxide, 16.6% with placebo and 11.1% with meprobamate. Signs of motor retardation were particularly high with chlorpromazine, seen in 10 out of 25 patients. Meprobamate used at the dosage of 600 mg/day, half the usual dosage, was no more effective than placebo. At conventional dosages both chlordiazepoxide and chlorpromazine showed a profile of drug activity which included global psychiatric improvement, reduction of manifest anxiety, fewer subjective patient responses indicative of anxiety, higher dropout rate (originally started with 174 patients), and a higher incidence of somatic side reactions.

Department of Psychiatry
State University of New York
Downstate Medical Center
Brooklyn, N.Y.

3019 Michaux, Leon, Duche, D., & Perpiniotis. Etude pharmacodynamique, clinique et thérapeutique du G 22,355 en pèdo-psychiatrie. [Therapeutic and clinical pharmacodynamic study of G 22,355 in child psychiatry]. *Third World Congress of Psychiatry Proceedings*, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 927-929.

Imipramine in 25 mg p.o. or i.m. doses was used in 13 children, 9-16 years of age, for an average period of 6 weeks. Five had depression, 4 obsessional syndrome and 4 miscellaneous states. The dosage was progressively increased to a maximum of 75 mg, rarely 100 mg/day. Good results were obtained in 4 cases of depression, 3 cases of obsessional syndrome, 1 case of tic and 1 hysterical-type reaction. Slight improvement was obtained in 3 cases: 1 atypical depression, 2 obsessional syndrome. No improvement was obtained in 1

case of inhibition. EEG surveillance was maintained throughout. Tolerance was excellent. [No address]

3020 Rothman, Theodore, Grayson, Harry, & Ferguson, James. A comparative investigation of isocarboxazid and imipramine in depressive syndromes: autonomic measures. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress Psychiatry Proceedings*, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 937-941.

Sixty-four male depressives, aged 30-60 years, most showing suicidal tendencies were treated with isocarboxazid, imipramine or placebo. There were 23 cases of schizophrenia, 4 were schizoaffective, 25 had endogenous or manic depression, 7 had personality disorders and 5 had psychoneuroses. Isocarboxazid was given in an initial dose of 40 mg daily reduced to 20 mg; imipramine was given initially at 100 mg daily and gradually reduced to 50 mg; the placebo was administered 3 times a day and eventually reduced to once a day. The patients were placed on their treatment regimen for a period of 10 weeks. Laboratory tests, tests of autonomic function, EEG's, MSRPP, a battery of psychological tests and scales, facial photographs of the patient smiling and reposed, the Rothman's Symptom Check List and other tests were applied. An $\bar{A}$ score was derived by combining weighted standard scores of 7 measurements: viz, salivary output; sublingual temperature, heart period while reclining, diastolic blood pressure while reclining; volar skin conductance while reclining; palmar skin conductance while straining and a ratio of palmar conductance measured while reclining to that measured while straining. For unselected populations the $\bar{A}$ is distributed normal and this mean is defined as "autonomic balance." Patients with depressive syndromes have $\bar{A}$ scores indicating that the direction of movement is towards the sympathetic branch of the autonomic nervous system. Those patients treated with a drug show: a) isocarboxazid as an $\bar{A}$ score showing a parasympathetic direction; b) placebo showed less parasympathetic dominance than isocarboxazid; c) imipramine shows sympathetic dominance. Patients treated with placebo showed measurable change. There is a correlation between the parasympathetic dominance as shown by the $\bar{A}$ scores which cuts through treatment procedures when improvement occurs. Global evaluations may

be more sensitive indicators of behavioral changes than the individual psychological tests and ratings.

University of Southern California
School of Medicine
Los Angeles, Calif.

3021 Szara, Stephen. Psychological effects and metabolism of N,N-diethyltryptamine, an hallucinogenic drug. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 670-673.

N,N-dimethyltryptamine (DMT) was administered in the same dose, 1 mg/kg i.m. to 10 normal volunteers and 10 chronic schizophrenics. Thirty minutes after injection the subjects were scored on the Abramson-Jarvik scale and the Quantified Psychiatric Mental Status Scale. Between 60-90 minutes after injection, a battery of psychological tests were administered including reaction time, digit span, etc. At 90 minutes subjects were again scored on both scales and all sessions were tape recorded. Urine was collected on arising, just before injection and at 3, 6 and 9 hours after injection. 6-Hydroxy-N,N-diethyltryptamine (6HDET) and indole acetic acid were assayed. A positive correlation between the amount of 6 hydroxylated metabolites of Det, a hallucinogenic drug, and psychological effects was established. The 6-hydroxy metabolite appears involved in the production of psychological changes. A delayed excretion curve for this metabolite was demonstrated in schizophrenic patients. 6-Hydroxylation may have a possible role in producing psychotoxic metabolites endogenously.

[No address]

3022 Freedman, Daniel X. Studies of LSD-25 and serotonin in the brain. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 653-658.

Fourteen chronic schizophrenic women received 10 mg of reserpine as a single dose and 2 days later the only sign of an altered brain milieu was the miosis. They then received 120 µg of LSD and showed prolonged and toxic reactions: marked tremor and akathisia in the majority, and in 1, an oculogyric crisis. Each felt the drug was less pleasant than her control LSD and that the effects lasted longer. With the exception of pupil size, tolerance developed normally. LSD and related psychotomimetics appeared to effect both the level and distribution of biogenic amines in the brain and the alteration of normal rates of binding and release leads to different behavioral, autonomic and chemical response to such drugs.

Yale University School of Medicine
New Haven, Conn.

3023 Gamma, G., Gobbi, L., Ferrio, L., Rivolta, A., Gandiglio, G., & Vercellino, F. Contributo clinico, elettroencefalografico e biologico allo studio della psilocibina [Clinical, EEG and biological contribution to the study of psilocybin.] Sistema Nervoso, 1962, 14, 389-408.

Five nondeteriorated chronic paranoid schizophrenics and 5 affective depressive psychosis cases were given 2 and 8 mg doses of psilocybin respectively, p.o. for 10 days. Eleven volunteers, including 1 normal subject (male medical student) and 10 females of various psychiatric diagnoses were given i.v. doses of 3-9 mg psilocybin. In the 1st experiment psychomotor changes were noted ranging from excitation to psychonudism with, generally, aggravation of the EEG. Most subjects showed almost constant mydriasis, tachycardia, and irregular pressor effects, with the manifestation of some elation. The normal subject saw kaleidoscopic colored hallucinations. Variations in alpha wave rhythm were noted in some subjects, along with psychomotor unrest. Psilocybin is of value in revealing psychopathological structures and personalities.

Ospedali Psichiatrici Provinciali di
Torino
Torino, Italy

3024 Jacquin, Maurice. Etude du Tofranil 10 en psychiatrie gerontologique. [Study of Tofranil in gerontological psychiatry.] Strasbourg Medicale, 1962, 13, 790-793.

Thirty-four patients in the following categories were studied: female, aged 60 years or over, chronic psychotics in advanced stages of their illness, showing some signs of depression associated with other psychiatric symptoms. Usual daily dosage was 20 mg imipramine (Tofranil). In some cases, 3 weeks after beginning of treatment, it was raised to 10 mg t.i.d., and maintained for over 5 months. Good results were obtained in 12 (35%) of these patients, thus encouraging the use of higher dosages.

Hôpital Psychiatrique de Hoerdt
(Bas-Rhin), France

3025 Janke, Von W., & Schmatzer, Elisabeth. Experimentalpsychologische Untersuchungen zur Wirkung einer Prothipendyl-Cyclobarbitall-Calcium-Kombination im Vergleich zu Cyclobarbitall-Calcium und Placebo. [Experimental psychological studies on the effects of a prothipendyl-cyclobarbitall-calcium combination in comparison with cyclobarbitall and placebos.] Arzneimittelforschung, 1962, 12, 1031-1036.

The effects of Itridal were evaluated in 2 series of tests, each comprised of 5 males and 5 females, 20-30 years of age, to determine depth of sleep, performance capacity, and subjective sensations. Each of 3 dosage regimens was administered before sleep: 2 tablets consisting of either Itridal (40 mg prothipendyl and 200 mg cyclobarbitall calcium), cyclobarbitall calcium (400 mg), or placebo. Depth of sleep (determined from movements during sleep) was equal for both drugs but differed from placebo in that the depth of sleep was increased over a period of several hours. Psychological and psychomotor tests showed marked differences between Itridal and cyclobarbitall calcium. Following cyclobarbitall, impairment of performance was observed in reaction time and psychomotor coordination. Itridal did not differ from placebo in this respect.

Institut für Psychologie
Universität Marburg/Lahn
Marburg/Lahn, Germany

3026 Smith e Incas, Jaime, Frazier, Robert L., & Patterson, Ralph M. The treatment of depression with meprobamate-benactyzine (Deprol). Evaluation of a "sliding scale" method of dose selection. Journal of the National Medical Association, 1962, 54, 472-475.

Deprol (400 mg meprobamate and 1 mg benactyzine) 4-10 tablets/day p.o. was administered to 62 depressive patients, aged 17-77 years, for 7 weeks to 10 months. Positive results ranged from good to excellent in all patients. Dosage adjustment was based upon initial response, with a sliding scale of dosage selection recommended. Remission was generally observed in 9-12 days.

Orient State Institute
Columbus, Ohio

3027 Gratton, L., Houde, L., Lafontaine, R., & Fournier, G. "Syndromes hypermoteurs et trifluoperazine". [Hypermotor syndromes and trifluoperazine.] Canadian Psychiatric Association Journal, 1961, 6, 257-260.

Thirty-three boys, aged 7-12 years, were divided into 3 groups of 11 for study purposes: administration of the Bender-Gestalt, Goodenough, and Draw-a-Tree tests in relation to the effects of trifluoperazine on ego functions and ego structuration in hypermotor syndrome. One group was given trifluoperazine, the 2nd group, placebo, and 3rd group, no medication. Trifluoperazine and placebo were prescribed at a dose of 0.5 mg/10 lbs of body weight/day. The doses were increased when needed after 2 weeks, at a ratio of 0.25 mg/10 lbs. The tests were repeated after 2 months, and the children were seen regularly for 5-10 minutes once a week; a complete observation form was filled out every 2 weeks by the nurses and psychiatrists. Poor results were obtained in Group I, but this was found to be due to the drug's opposite effects on 2 types of hyperkinetic children. In graphs with the level of motor activity on the ordinate and days of treatment on the abscissa, "Type I children" showed a curve with wide fluctuations. Children of this type showed corresponding variations in motor activity with apparently

normal neurology and no sign of anaclitic depression. They responded well to trifluoperazine with a mild akinesia, improved handwriting changes, and a decrease in motor activity. This type of hyperactivity provides an indication for trifluoperazine and small doses are sufficient. In "Type II children" the curve is relatively flat and clinically these patients exhibit flat affect, depression, and all have extrapyramidal syndromes which were not associated with the chemotherapy. Trifluoperazine appears contraindicated in these children, as it showed a tendency to worsen their hyperactivity.

Service de Psychiatrie Infantile
Hôpital Ste-Justine
Montreal, Quebec
Canada

028 Renaud, J., Quarti, C., & Netter, A.
G 33 040 en médecine psychosomatique.
G 33040 in psychosomatic medicine.] *Revue*
psychosomatique, 1962, 3, 737-751.

Trifluoperazine (G 33040) was used to treat pure psychosomatic cases, particularly psychogenic amenorrhea and depression, anxiety, psychasthenia, etc. (100-150 mg/day in divided doses) It was found contraindicated in anergic forms of depression. The drug was used to control sexual, emotional, and thymic tension in 8 women. The Robinson and Szondi tests were employed in evaluation. The low level of improvement and lessening of anxiety virtually negated practical interest, but the drug is recommended in depressive emotional crises or anxiety paroxysms in view of its antiadrenolytic action.

0, rue de Tournon
Paris 6, France

029 Simpson, George M., & Kline, Nathan S.
Histamine wheal formation and mental illness.
In: Cleghorn, R.A., Moll, A.E., & Roberts,
J.A. Third World Congress of Psychiatry
Proceedings. Volume II. Toronto/Montreal:
University of Press and McGill University
Press, 1962. Pp. 1010-1014.

Intradermal histamine produced a significantly smaller wheal in chronic schizophrenics than in acute schizophrenics, acute nonschizophrenics, and normal controls. The following drugs were used for 6 weeks: chlorpromazine, prochlorperazine, reserpine, imipramine,

and meproamate. Imipramine and prochlorperazine were both found to produce a significant reduction in histamine wheal formation in chronic schizophrenics.

Research Facility
Rockland State Hospital
Orangeburg, N.Y.

3030 Mariategui, Jaview, & Ramirez del Villar, E. Tratamiento de los cuadros depresivos con amitriptilina. [Treatment of depressive cases with amitriptyline.] *Revista de Neuro-Psiquiatria*, 1962, 25, 281-290.

Thirty-four cases of depression were treated with amitriptyline for 3-5 months. Usual dosage was 60-90 mg/day i.m. or 75 mg/day p.o. initially. Dosage was progressively raised to the average level of 100-200 mg/day. Complete remission was achieved in 35.3%, improvement in 29.4% and slight improvement in 20.6%. No change was observed in 8.8% and worsening, a swing towards mania, occurred in 5.9%. The drug is particularly beneficial in cases of endogenous depression. Its anxiolytic effect is stressed.

[No address]

3031 Cornil, J., Ajzenberg, D., & Mans, J. Contribution à l'étude du syndrome secondaire des neuroleptiques. Son traitement par le chlorhydrate d'orphenadrine. [Contribution to the study of neuroleptic syndrome; its treatment with orphenadrine.] *Gazette Médicale de France*, 1961, 68, 2583-2585.

Orphenadrine (Disipal) was found useful in controlling neuroleptic-induced extrapyramidal disorder in 41 out of 56 patients. The case load included 20 men and 36 women. Fifty milligram tablets were used and dosage progressively increased, beginning with 100 mg/day reaching a maximal dose of 800 mg/day, most often optimal at 200-300 mg/day. In 16 cases there was a favorable potentiation of the neuroleptic effect (14 on chlorpromazine and 2 on levomepromazine).

[No address]

3032 Gelinet, M.M. Étude biologique et clinique d'un anorexigène: la diéthylaminopropiophenone retard. [Clinical and biological study of an anorexigen: slow-release diethylaminopropiophenone.] *Gazette Médicale de France*, 1962, 69, 821-823.

Derfon tablets (0.025 g diethylpropion) were given t.i.d. or q.i.d. to over 11 obese patients, 12-74 years of age. Diethylpropion was perfectly tolerated in spite of coexisting diseases such as diabetes, psychiatric disturbances, etc. and was compatible with other medications given these patients. Results were consistently good in relation to weight loss, on the average, 4 kg a month and 1-1.5 kg in 8 days. However 3 failures were recorded. No significant changes in urinary metabolites were noted except for a slight increase in glomerular filtration.

College de Médecine des Hôpitaux de
Paris
Centre d'Endocrinologie
Hôpital Laennec
Paris, France

3033 Schenker, Victor J., Marjerrison, Gordon, Schlachet, Peter, Feedman, N., Hankoff, L.D., & Engelhardt, D.M. Monoamine oxidase inhibition and antidepressive correlates. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 642-649.

Nineteen male patients (reactive depression, involutional psychosis, psychoneurosis, schizophrenia with depression) were randomly assigned to pheniprazine (12 mg orally each day at 10 A.M.) or placebo. MAO inhibition was assessed spectrophotofluorometrically by increase of urinary tryptamine. The Abbreviated Depression scale of the MMPI, the Clyde Mood Scale, Digit Symbol test, perseveration tests, Wechsler Memory Scale, time estimation, tapping test, work association tests and WAIS vocabulary as well as the Bender Visual-Motor Gestalt Test, the TAT, Rosenzweig Picture Frustration test, childhood memories and the Rorschach test were used in evaluation. The inhibitor produced a distinct effect in the alleviation of depressive symptomology which could be objectively described in psychiatric testing, and the drug induced alleviation could be correlated with biochemical response to the drug. Lack of clinical

improvement showed a lower index of MAO inhibition.

State University of New York
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3034 Resnick, Oscar, Krus, Donald, Raskin, Milton, Rivera, Milagros, & Freeman, Harry. The effect of pretreatment with monoamine oxidase inhibitors on reserpine action in normal subjects and in schizophrenic patients. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 638-642.

Six normal male subjects were given 1.25 mg reserpine i.m. and 2 days later were put on 20-50 mg isocarboxazid for 2 weeks. On the 14th day they received another 1.25 mg reserpine injection. One hour after administration of reserpine, flushing, a feeling of warmth, a "big-head" feeling, headache, nasal congestion and sniffles, bronchial constriction, miosis, bloodshot eyes, gastritis, and lowered blood pressure were noted. Mild sedation usually was noticed about 2 hours after the injection. The same dose, given after 2 weeks of isocarboxazid therapy, produced the same effects, but they were much more pronounced and prolonged. This was especially true for sedation and tranquilization. The level of apparent eye horizon was raised in all cases. One subject, a very good bowler, complained that his score was very low while on isocarboxazid. Reserpine alone has a biphasic effect on the apparent eye horizon--a rise followed by a fall. Ten weeks after these trials 3 subjects were placed on nialamide, 100 mg/day. On the 14th day the subjects received the same 1.25 mg reserpine dose i.m. Nialamide did not raise the apparent eye horizon, but produced a biphasic response. Also, there was no lowering of blood pressure, and in 2 subjects systolic blood pressure actually rose. Nialamide, unlike isocarboxazid, may have produced a rise in the concentration of both 5HT and catecholamine centrally and peripherally. Four schizophrenics received 150 mg iproniazid

per day for 6 weeks and were then given 3 mg reserpine i.m. as a single dose. The patients were observed for 3 days and then took placebos for 4 weeks followed by similar reserpine treatment. Additionally, 3 depressives on phenelzine and 1 on isocarboxazid were given a single 3 mg reserpine dose i.m. All 8 patients showed typical somatic and central responses to the reserpine. Pretreatment with iproniazid, isocarboxazid, and phenelzine in psychotics may potentiate the sympatholytic and sedative effects of reserpine.

Worcester Foundation for Experimental
Biology
Shrewsbury, Mass.

3035 Scarpalezos, S. Aspects psychiatriques particuliers de la porphyrie aigue. [Psychiatric aspects relating to acute porphyria.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 630-633.

Six cases of acute porphyria were treated with calcium, insulin, liver extract, vitamins and adrenal cortex extract [dosage unspecified] with some success.

Athens, Greece

3036 Cochrane, Carl M., Prange, Arthur J. Jr., & Abse, D. Wilfred. Reserpine-produced changes in the direction of aggressive drives. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 370-373.

Patients suffering severe personal discomfort or causing difficulties in ward management were randomly assigned to a double-blind study in which they received either: 8 mg reserpine for 2 days and then 4 mg daily; 600 mg chlorpromazine for 2 days and then 300 mg daily; 120 mg powdered opium initially and then 60 mg, or placebo. The chief measurements were the MMPI and a checklist of behavioral observations filled out by the psychiatric nurses. A percent

aggression score was worked out equal to "aggression score"/"aggression inward score plus aggression score." As the percentage rises, more tendency toward aggressive expression is indicated. The MMPI correlated satisfactorily with the checklist measures of percent aggression. Reserpine cases showed an increased tendency toward aggression, while placebo cases showed a slight shift toward more inhibition and anger-dominance. Reserpine causes patients to show moderation in behavioral organization in the direction of a greater dominance of aggressive, and perhaps generally alloplastic, behavior. If reserpine causes a shift towards freer aggressivity, it follows that a patient whose symptoms already betray an anger-dominance should not be considered as improving and is probably getting worse. However, a patient who shows a premedication adjustment of inhibition and anger-intype symptoms should be considered improving if he moves towards freer drive expression. In the reserpine group 71% of the initially low percent aggression cases were drug-successes compared to only 27% of the initial high scores. The direction of success was reversed in the placebo group. Of the patients given placebo only, 14% of those initially low were successful drug cases while 57% of those scoring high were in this category. Improvement on reserpine could be predicted in 72% of cases while for placebo the prediction accuracy was only 26%.

University of North Carolina
Chapel Hill, N.C.

3037 Jus, Andrzej. Conditioned reflex experimental research in the evaluation of action of some psychotropic drugs. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 151-155.

Observations were carried out on 202 patients comprised of 167 schizophrenics, 8 manic-depressives, 15 patients with involutional psychosis, 5 with posttraumatic psychosis and 7 with psychoneurosis. The following methods of treatment were applied: insulin coma - 85 patients, chlorpromazine - 35 patients, reserpine - 18 patients,

thiopropazine - 20 patients, haloperidol - 5 patients, benactyzine - 3 patients and nialamide - 33 patients. Polygraphic reactivity studies were applied to 136 of these patients with simultaneous observation of UR's and CR's in the ECG, neurogram and electrodermogram (psychogalvanic reactions). Hypoglycemia was also assessed. Numerous remarks are made on CR experiments in the course of pharmacological treatment. In some psychoses, but not all, the appearance of a CR is a very sensitive indicator which can presage an improvement long before it may be seen clinically. For instance in states of catatonic stupor during treatment by insulin coma or by neuroleptics, the appearance by conditioned alpha blocking with acoustic stimuli as CS and light as reinforcement can be observed. This conditioning appeared in patients who improved clinically only later.

Academy of Medicine
Warsaw, Poland

3038 Brune, Guenter G., Pscheidt, Gordon R., & Himwich, Harold E. Correlations between the behaviour of patients with mental disturbances and effects of psychoactive drugs on some urinary products. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 111-117.

Behavioral changes wrought by therapeutic doses of reserpine and isocarboxazid on 12 patients (9 schizophrenia and 3 mental deficiency) were studied in relation to changes in 5HT and levarterenol metabolism. Twenty-four hour urine specimens were collected for each patient and the following indole metabolites were measured: 5HTAA, total 3-indoleacetic acid and tryptamine. Levarterenol and epinephrine were also assayed. Four schedules were used: placebo, 4 mg reserpine/day or 30 mg isocarboxazid/day, 4 mg reserpine plus 30 mg isocarboxazid/day followed by a placebo. Patients were kept on a constant-intake protein diet, i.e., tryptophan intake was kept constant, during the 47-day observation period. A close relationship between the degree of psychotic behavior and the amounts of indole metabolites eliminated in the urine existed.

Thus the level of urinary indoles does not correlate with the nosologic classification of schizophrenia but with the intensity of schizophrenic symptoms. Increases of indoles sometimes preceded the activation of psychosis and always accompanied behavioral aggravation. Rises in urinary epinephrine and levarterenol level occurred with the onset of signs of increased anxiety and were not associated with psychotic activation unless this was accompanied by anxiety.

Galesburg State Research Hospital
Galesburg, Ill.

3039 Ayd, Frank J., Jr. Long-term imipramine therapy: clinical and laboratory observations. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 913-915.

One-hundred patients, aged 36-72 years (14 chronic depressive, 22 chronic relapsing manic depressive, and 64 manic depressive or involutional melancholic) were treated with imipramine, beginning with 150 mg/day, sometimes increased to 200 mg for 3-6 months, after which the dose was gradually reduced to a maintenance level or the drug was withdrawn completely. The 64 manic depressives and involutional melancholics took imipramine for 9 months to 2 years before a full remission was obtained. Imipramine may cause idiosyncratic reactions such as dermatitis, jaundice, and agranulocytosis; there were no allergic reactions. Every patient had some type of anticholinergic effect, especially blurred vision, dry mouth, and constipation. With continued administration, action was moderated or tolerance developed. In normotensive and hypotensive patients, imipramine had no effect on blood pressure. These patients took a total of 21,600-170,150 mg imipramine. It can be administered for prolonged periods even in large doses without risk of harmful effects on the blood and liver. Maintenance doses can be used to obviate further depression in patients subject to repeated attacks of melancholia.

patients subject to repeated attacks of melancholia.

Franklin Square Hospital
Baltimore, Md.

3040 Dunlop, Edwin. Selective therapy in depression. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 870-874.

ECT, an antidepressant or combined drugs have been evaluated in approximately 1,000 patients over a 10-year period for selective therapy on the basis of their autonomic nervous system responses to epinephrine and methylcholine. The epinephrine response reveals components of anxiety and tension, which indicate the combination of a tranquilizer with an antidepressant, and the methylcholine response (systolic), when maximal, indicates the use of an antidepressant. The latter test is continuously recorded on an automatic blood pressure follower. The information is prognostic rather than diagnostic. Five case histories are presented and information on isocarboxazid, nialamide, etryptamine, imipramine, amitriptyline, meprobamate, benactyzine and tranquilizers, e.g., fluphenazine, chlorprothixene, chlordiazepoxide.

9 School Street
Attleborough, Mass.

3041 Schon, Martha, Sutherland, Arthur M., & Rawson, Rulon W. Hormones and neuroses - the psychological effects of thyroid deficiency. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 835-839.

Psychological manifestation of thyroid deficiency and the changes following the administration of thyroid products were studied in 24 patients (21 females and 3 males) with hypothyroidism but no gross emotional disturbance. The Wechsler-Bellevue Intelligence Scale (vocabulary tests), Memory Span for Digits, Block Design Test and the Thurstone Temperament

Schedule were used in evaluation. After administration of thyroid medication [unspecified], most of the abnormal behavioral symptoms (irritability, lethargy) decreased or disappeared, and the patients returned to a state of general well being. They achieved a significantly higher score on the Block Design Test after treatment, but the time required to carry out the task was not affected. The patients' memory for digits improved, retention for digits backwards being mainly affected. Temperament tests showed that they were more capable of taking the initiative, that they had a more even disposition, were less irritated, could concentrate better and were more cooperative. However, the changes were not statistically significant and this appears to indicate that interviews were more reliable than the testing data.

Memorial Sloan Kettering Cancer Center
New York

3042 Véziris, C.D. Données récentes sur la ménopause. [Recent data on menopause.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. - Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 353-366.

Menopausal patients were examined for FSH excretion levels. Of women recently past menopause, 30 had normal FSH levels while 15 had higher than normal levels. Seven out of 104 women who had passed menopause for about a year and a half had normal levels while the rest showed higher than normal FSH levels. Treatment with di-enestrol and similar products was beneficial, alleviating stress in some cases and causing a diminution in histamine and acetylcholine levels.

[No address]

3043 Contini, Paolo. Esperienze geriatriche con un nuovo neurostimolante: 1'l-fenil-2-pirrolidinopentano. [Geriatric experience with a new neurostimulant: 1 phenyl-2-pirrolidine-pentane.] *Settimana Medica*, 1962, 50, 815-823.

Dillescno (10 mg 1-phenyl-2-pirrolidine pentane combined with vitamins) was given to 23 patients, 60 years and older, 1 tablet t.i.d., usually for 10-20 days. Patients fell into 2 categories: arteriosclerotic, general asthenia in acute convalescence patients, and chronic depression. Eight patients showed improvement and 10 slight improvement. The drug seems to be a suitable psychotonic for the aged and tolerance has been excellent.

Istituto de Gerontologia
Università degli Studi di Firenze
Florence, Italy

3044 Goldman, Milton S. Experience with antidepressants in general practice. *Journal of the Florida Medical Association*, 1962, 45, 727-729.

Isocarboxazid was given to a random series of 65 outpatients, all females, with the following diagnoses: endogenous depression, agitated depressive reactions, reactive depressions, postmenopausal involutional depressions and manic depressive in the depressed phase. Four also complained of angina pectoris. All received 10 mg t. i. d. for the 1st week, reduced to 10 mg in the morning and at bedtime thereafter. Excellent to good results were obtained in 82%, and 92% showed excellent, good or fair results. Three out of the 5 failures were in the endogenous depression group (38 cases). The response in 20 out of 21 patients with postmenopausal depression was good to excellent. Minor side effects were nausea (5 mild, 2 severe), anorexia (3 mild) and insomnia (8 mild and 1 severe).

1680 Meridian Avenue
Miami Beach, Fla.

3045 Trillot, J., & Noyer, J. Melancolia anxieuse actions respectives de l'electrochoc et de la chimiotherapie. [Anxious melancholia - the effects of electroconvulsive therapy and chemotherapy.] *Toulouse Medical*, 1961, 63, 417-419.

A 58-year-old woman suffering from agitation with anxiety, insomnia and suicidal thoughts was treated with imipramine and meprobamate in increasing doses [dosage unspecified]. The patient improved but later became delirious, speaking of ideas of damnation. Two ECT courses cured this patient.

[No address]

3046 Mouren, P. Le traitement de l'insomnie. [Treatment of insomnia.] *Marseille Médicale*, 1962, 99, 481-486.

The more common hypnotics are barbiturates, non-barbituric hypnotics, such as methylpentynol, phenyl-ethyl-glutarimide, which do not cause addiction, neuroleptics such as chlorpromazine and some antihistaminics, such as promethazine. Adjunctive drugs include autonomic sedatives, bromides and hypnotics with an aldehyde or ketone radical. The type of drug and doses chosen must be related to the type of insomnia, i.e., initial, terminal, or intermittent, and according to its etiology, i.e., whether primary or secondary. Initial doses should be small and products should be as atoxic as possible.

[No address]

3047 Milligan, W. Liddel. Treatment of depression. By a combination of tranlycypromine and trifluoperazine. *Medical Proceedings*, 1962, 8, 237-240.

Parstelin (10 mg tranlycypromine and 1 mg trifluoperazine b.i.d., p.o.) was administered to 500 patients (130 endogenous depression, 180 reactive depression, 90 involutional melancholia, 40 schizoaffective depression and 60 senile depression), aged 20-82 years, for an average of 9 months. Results were excellent in 233, good in 99 and slight in 168. Side effects, mild in all but 2 instances, included insomnia, headache, dizziness, metallic taste,

weakness, etc. Overall, 66% improvement resulted with Parstelin. A pilot study with 30 obsessional psychoneurotics who received secobarbital (3/4 grain t.i.d. for 3 weeks), then trifluoperazine (5 mg b.i.d. for 3 weeks) and Parstelin revealed significant improvement with Parstelin unobtainable with either of the other drugs.

Royal Medical Psychological Association
Portsmouth, Great Britain

3048 Levinson, B.W. The person behind the pill. Reflections on the new look in depression. Medical Proceedings, 1962, 8, 374-377.

Tranlycypromine (10 mg b.i.d.) or Parstelin (10 mg tranlycypromine and 1 mg trifluoperazine, b.i.d.) was administered to 50 depressive patients, aged 20-70 years for 8 months. Parstelin was given to combat concomitant anxiety or agitation. Results included 40 who displayed marked improvement, 8 moderate improvement and 2 no improvement. Side effects occurred in 6; 3 had dizziness, 2 muscle twitches and 1 impaired micturition. Symptoms of depression were alleviated in 40 patients within 48 hours. Additional ECT was required by 13.

Johannesburg
Union of South Africa

3049 Gould, Arnold H. Combined dexbrompheniramine-fluphenazine (Diperm Chronotab) in the oral treatment of pruritus. Journal of New Drugs, 1962, 2, 179-182.

Diperm (6 mg dexbrompheniramine and 0.5 mg fluphenazine) was administered b.i.d. to a preliminary series of 34 patients with pruritus, and t.i.d. to 10 healthy adult volunteers for 30 days. Laboratory tests revealed no deviation from normal limits, and patients were symptomatically improved. For definitive evaluation of the combination drug as an oral antipruritic, Diperm or trimeprazine (5 mg b.i.d.) was administered on a double-blind basis to 97 patients with diverse itching dermatoses, for a total of 144 trials. Forty-seven patients had 5-day crossover trials of both drugs, with a treatment-free interval of 48 hours between trials. The remainder participated in double-blind trials

for 7-14 days. Complete or marked relief of itching was observed in 85% with Diperm and 59% with trimeprazine. No antipruritic effect was apparent in 6% with Diperm and 30% with trimeprazine. Minor side effects, primarily mild drowsiness, occurred in 10% of both drug groups. The Diperm repeat-action tablet, at a dosage of 1 tablet b.i.d. appears to be an effective and generally well tolerated preparation for the oral treatment of itching.

Division of Dermatology
Department of Medicine
Georgetown University School of Medicine
Washington, D.C.

3050 Fullerton, A.G., Boardman, R.H., Bethell, M.S., & Conway, Stella. Neurotic and mild psychotic depression: combined drug treatment of the target-symptom. Chemotherapy Review, 1962, 2, 38-40.

The initial dose of Parstelin (1 mg trifluoperazine and 10 mg tranlycypromine) generally was 1 tablet t.i.d., and if tolerated, it was gradually increased. Maximal daily dosage reached 6 tablets per day. Of the 60 patients treated for mild depression, 43 (70%) benefited satisfactorily and 17 (30%) either received minimal benefit or none. Faintness, drowsiness, blurred vision, urgency of micturition and diminished libido (3 males), sudden severe occipital headache in 11 patients and mild parkinsonism in 1 patient on 6 tablets a day were listed as side effects.

Gerrison Hospital
Dorchester
Dorset, Great Britain

3051 Dorison, Ezra E., & Blackman, Sheldon. Imipramine in the treatment of adult enuretics. American Journal of Psychiatry, 1962, 119, 474.

Thirty soldiers, aged 17-23 years, referred to a clinic because of enuresis were studied in a double-blind trial where 50 mg imipramine was given to half the subjects at bed time, while the other half received a placebo. After 2 weeks, of the 15 subjects in the medication group, 6 reported improvement. Eleven of the 15 in the placebo group

reported improvement. None of the 30 subjects reported any worsening of their condition.

Mental Hygiene Consultation Service
Fort Knox, Ky.

3052 Letailleur, Maurice, Monnerie, Rene, Colas, Yves, & Vinyes. Chlorpromazine et gestation. [Chlorpromazine and gestation.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 367-373.

A 22-year-old woman suffering from hallucinations was given various psychiatric treatment including ECT, trihexyphenidyl, and chlorpromazine over a period of some 4 years. She received no less than 150 mg/day chlorpromazine throughout most of a pregnancy. She delivered a female child weighing 4.06 kg under normal circumstances. The child was normal, and psychological and psychomotor development was in no way unusual. The placenta showed a chlorpromazine recovery level of 2.5 mg/kg/ while no chlorpromazine was detectable in the umbilical cord (sensitivity of method ca 0.5 mg/liter).

Clinique de Neuropsychiatrie de
Clermont-de-l'Oise
Clermont-de-l'Oise, France

3053 Bruyn, G.W. Thiopropazate dihydrochloride (Dartal) in the treatment of Huntington's chorea. Psychiatria, Neurologia, Neurochirurgia, 1962, 65, 430-438.

Choreatic hyperkinesia were reduced in 1, markedly reduced in 2 and practically eliminated in another out of 4 patients suffering from Huntington's chorea who received 2-20 mg thiopropazate t.i.d. Findings relating to urinary excretion of copper and amino acids as well as serum ceruloplasmin were essentially normal in all patients with the exception of a slightly raised amino acid excretion in 1 (no

significance). Both thiopropazate and perphenazine are considered drugs of choice in Huntington's chorea.

Neurological Department
Institute of Neurological Sciences
University Hospital
Leyden, The Netherlands

3054 Musaph, Herman, & Van Loggem, Manuel. Research of chlordiazepoxide (Librium) into normal subjects and neurotics with pathological itching states. Psychiatria, Neurologia, Neurochirurgia, 1962, 65, 402-423.

Twenty neurotic patients, treated for pathologic itching, and 25 normal persons were tested before and after 10 mg chlordiazepoxide p.o. Ten patients were studied on a double-blind basis. The assessment test used was the Van Loggem test (4 pictures representing love and sexuality, loneliness, aggression, and social contact with many people). Chlordiazepoxide may make patients more indifferent, anxiolytic effects resulting from a so-called "declutch" mechanism. The drug caused improvement of basic mood and decrease in fear. No striking differences were found between normals and neurotics. While not a specific antipruritic drug, it may break through a vicious cycle and allow better psychotherapy.

[No address]

3055 Horne, P.M., & Forrest, A.D. Pilot trial of I.C.I. 31397. A new mono-amine oxidase inhibitor. Scottish Medical Journal, 1962, 7, 224-229.

In a pilot study, α -methylbenzylhydrazine (I.C.I. 31397; 3-20 mg/day) was administered to 24 depressive patients aged 24-72 years for 10 days to 12 weeks. Evaluation by psychiatric assessment and a 3-point rating scale at 2 weeks revealed 62.5% patient improvement, with optimal dosage lying between 10-30 mg/day. Abnormal cephalin cholesterol flocculation tests were manifested by 2 patients during treatment, a fact which suggests

epatotoxic sequelae. Overall, 15 patients improved with I.C.T. 31397 and 9 did not.

Royal Edinburgh Hospital for Mental Disorders
Edinburgh, Scotland

56 Simpson, R. Wallace & Tolmie, J.B. Clinical assessment of trifluoperazine in psychotic illness. Medical Proceedings, 1962, 8, 108-114.

Trifluoperazine (10-20 mg/day p.o.) was administered to 177 patients, average age 28 years (33 puerperal psychotics and 144 schizophrenics) for up to 2 years. Of the schizophrenics, 75% (108) improved, with 34% (9) showing marked improvement with partial complete regaining of insight. Side effects constituted minor extrapyramidal symptoms, restlessness, akathisia and dyskinesia, all controllable by dosage adjustments and orphenadrine.

Bedford Manor Hospital
Maidenhead, Great Britain

57 Silver, E. The treatment of psychomotoric depressive states. A comparison of imipramine hydrochloride with tranlycypromine and trifluoperazine. Medical Proceedings, 1962, 8, 251-256.

Imipramine (150-200 mg/day p.o.) was administered to 59 depressed patients, average age 44 years, while 50 patients, average age 44 years, received Parstelin (1 mg trifluoperazine and 10 mg tranlycypromine; 3-4 tablets/day). Many patients evidenced remarkable improvement after only 3 days. With imipramine, 47 responded satisfactorily, without side effects, greater duration of treatment, and increased expense diminished drug efficacy. Depression was alleviated most dramatically with Parstelin in 38 patients. The combination drug appears to be vastly superior to imipramine alone.

to address]

58 Dandiya, P.C., & Sharma, J.D. Studies on Acorus calamus. Part V. Pharmacological actions of asarone and β -asarone on central

nervous system. Indian Journal of Medical Research, 1962, 50, 46-60.

Asarone and β -asarone, recently isolated active principles of Acorus calamus, are psychoactive drugs. Asarone and β -asarone (50 mg/kg i.p.) prolonged sleeping time in mice induced by pentobarbital (40 mg/kg i.p.) hexobarbital (100 mg/kg i.p.), or ethanol (3g/kg i.p.). Lysergide (1 μ g/kg i.p.) and iproniazid (150 mg/kg i.p., t.i.d.) failed to influence the hypnotic potentiating property of asarone and β -asarone (50 mg/kg i.p.). Both asarone and β -asarone produced significant reduction in the rectal temperature of 80 mice. Neither asarone nor β -asarone exhibited analgesic activity. β -asarone appeared to facilitate electroshock while asarone revealed a slight protective influence. Asarone (25-50 mg/kg i.p.) effectively protected mice against 70 mg/kg pentetrazol s.c. conclusions, while β -asarone enhanced pentetrazol toxicity. Picrotoxin (2 mg/kg s.c.) convulsions were facilitated by both drugs, while strychnine (0.3 mg/kg s.c.) convulsions were not influenced by either drug. Neither drug induced ataxia. Both agents exerted a taming influence on hostile cats as indicated by Norton and de Beer's "sociability" scores. β -Asarone specifically blocked CAR's in rats. Asarone produced comparable results at lower dosages.

Department of Pharmacology
S.M.S. Medical College
Jaipur, India

3059 Theodorides, M.M. Essai du bromométhylate de α -pyrrolidinopropionyl-phénothiazine (Diaspasmyl) en pédiatrie. [A test of α -pyrrolidinopropionyl phenothiazine bromomethylate (Diaspasmyl) in pediatrics.] Journal de Médecine de Bordeaux, 1962, 139, 459-464.

α -Pyrrolidinopropionyl phenothiazine (Diaspasmyl) was administered to a group of 23 infants who suffered from vomiting (12 otorhinolaryngeal or bronchial cases, 9 gastroenteritis cases, and 2 pyloric stenosis cases), either orally (2-2.5 mg/kg), rectally (1-3 mg/kg) or s.c. (1-2 mg/kg). Mean duration of the therapy was 3 days. Cessation of the vomiting was attained in 20 cases, the other 3 failures consisting of the 2 stenosis cases and 1 case of intolerance. In addition, 12 successes were noted in all 12 cases of children 1-6 years old suffering from vomiting accompanying meningitis, or rhinopharyngeal or other disorders. Doses were 1-2 mg/kg orally, 0.5-1 mg/kg s.c., or 0.6 mg/kg i.v. Finally,

the drug was administered to 5 children suffering from acute dyspneic conditions, and in all cases the dyspnea was reduced clearly and rapidly.

[No address]

3060 Knoll, W. Gibt es neue Möglichkeiten der pharmakopsychiatrischen Behandlung? [Are there new possibilities in pharmacopsychiatric treatment?] Therapiewoche, 1962, 14, 545-547.

Sixty-seven female subjects were treated with Vesitan, a combination of thiopropazate and chlorphencyclane (1st 3 days: 1.5 cc i.m., t.i.d. or q.i.d.; thereafter, 2 tablets t.i.d.; after 3 weeks only 1 tablet t.i.d. or q.i.d.) The patients were hospitalized for catatonic conditions of excitement, hebephrenia, paranoid psychoses and symptomatic psychoses accompanying carcinoma, and for conditions of restlessness caused by arteriosclerosis. With the exception of a few cases, all patients had been ill for several years. In spite of these unfavorable conditions, 41 patients were so much improved that they could be discharged. Thirty-five out of these 41 were exclusively treated with Vesitan. The other 6 patients received Vesitan combined with ECT or with MAO inhibitors. Twelve psychotic patients, hospitalized for years, were improved and could be transferred from the violent ward. Nine patients showed no improvement; 4 showed increased restlessness and the medication had to be discontinued. Best results were seen in those schizophrenic processes where restlessness, anxiety, tension and delusions were factors. Side effects were minimal.

Psychiatrische Landeskrankhaus
Emmendingen/Bd, Germany

3061 Gore, Charles P., & McComisky, James G. A study of the comparative effectiveness of Librium, amylobarbitone, and a placebo in the treatment of tension and anxiety states. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 979-982.

Initially chlordiazepoxide (Librium) was given to 50 patients who complained of tension

or anxiety. The dosage was 30-80 mg/day in divided doses and the duration of treatment from 1 week to 4 months. Improvement of varying degree was reported by 80% of the patients and side effects (sleepiness or dizziness) were minimal. Then a trial group of outpatients suffering from anxiety was studied in a double-blind trial using 10 mg chlordiazepoxide, 50 mg amobarbital, and placebo. The trial period was 6 weeks and each medication including placebo was given for a 2-week period to every patient. Dosage was started at 20 mg chlordiazepoxide, 100 mg amobarbital, or placebo t.i.d. Chlordiazepoxide was most effective and no serious side effects were encountered.

Scaleshor Park Hospital
Burley-in-Wharfedale
Ilkley, Yorkshire
Great Britain

3062 Astrup, Christian. Conditional reflex studies of schizophrenics treated with ataraxic drugs. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 999-1001.

Three-hundred-and-six chronic schizophrenics, 178 acute and subacute schizophrenics, and schizophreniform psychotics were tested for CR's. One-hundred-and-fourteen of the patients received chlorpromazine, 14 reserpine, and 2 meprobamate. As a rule there were no essential differences in the experimental performances between pretreated and nontreated patients, which suggests that the effect of the schizophrenic process predominates over that of the anorexic drugs. Those treated with reserpine have less adequate responses and more inhibition of UR's than clinically matched cases not treated with drugs, but the differences were not statistically significant. In a group of 33 chronic schizophrenics, motor defense reflexes to electrical stimulation were carried out before and after drug administration. The effects of single doses of chlorprothixene, imipramine, tetrabenazine, chlorpromazine, prochlorperazine, and isocarboxazid were studied in 75 trials. Drugs showed a tendency to inhibit UR's. Chlorprothixene gave the most clear-cut inhibitory effect. In 311 schizophrenics treated with chlorpromazine, reserpine, meprobamate, prochlorperazine, and mepazine, the clinical effects were better when there were less pronounced disturbances of higher nervous activity. Severely deteriorated schizophrenics benefited

little from the drugs. In another series of schizophrenics treated with these and other drugs, no drug had a marked effect on severely deteriorated subjects. The problems of treating schizokinetic pathology should be further examined in order to obtain satisfactory results in hard core schizophrenics.

Bufts University School of Medicine
Boston, Mass.

3063 Dally, P. Anorexia nervosa - prognostic factors and the effect of treatment. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1019-1021.

ninety-seven cases of anorexia nervosa, including 2 men, were studied. Assessment of each patient's degree of recovery was made on a 14-point scale: 2 points for weight, regularity of menstruation, regularity of work, marital state, pregnancies, absence of worry over food or weight and absence of other psychiatric symptoms. Twenty-six patients scored less than 7 and were regarded as unimproved, 28 scored between 7 and 9 and were regarded as improved. Twenty-one patients scored 10 or more and could be considered to have made very good recovery. The majority of cases seemed to be obsessional neuroses but there was a secondary group suffering from anxiety hysteria, often with a mixture of depression. The most effective means of achieving weight gain was the result of a suggestion by Sargent of St. Thomas' Hospital. This consists of using very large doses of chlorpromazine combined with a modified insulin regimen. Patients are put to bed at the start of the illness and are told they must stay there until they have gained a definite weight. Chlorpromazine is given by mouth, starting with 200 mg/day and increased by 150 mg/day to the limit of tolerance. As much as 1600 mg/day has been given to difficult patients. It is essential to increase the chlorpromazine until the patient is virtually helpless to the point of not panicking at the sight of food; etc. Modified insulin therapy is also begun at once, starting with 10 U each morning and increasing until the patient sweats and becomes drowsy. Neither drug given alone produces as good results. Thirty-seven of

the patients were treated with chlorpromazine-insulin and regained weight. After weight has been restored psychotherapy may be needed to complete the cure, particularly in the anxiety-hysteria type of anorexia nervosa. The relapse rate was about 50% and these were readmitted within 6 months of leaving hospital. When early treatment is directed to restoring lost weight, the prognosis is less gloomy than many investigators would believe.

St. Thomas' Hospital
London, Great Britain

3064 Gabriel, Arthur N. A psychobiologic approach to the treatment of tics. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1050-1052.

Five cases are presented in which tics were successfully treated with psychopharmacologic agents (meprobamate up to 3,200 mg/day, chlorpromazine up to 800 mg/day and 4,000 mg/day, 200 mg imipramine/day) even in a treatment situation that concerns itself primarily with psychological factors.

[No address]

3065 Denham, John. Experimental approach to the treatment of schizophrenia. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1094-1096.

Chronic schizophrenics received 0.1 mg epinephrine and on the following day 10 mg mecholyl before, during, and after treatment with thioproperazine [dosage unspecified] on 3 separate occasions. The reactivity to epinephrine before treatment was found within normal limits in two-thirds of the patients while in the remainder it was reduced and short-lasting. Reactions to mecholyl were slight and short-lasting or absent in all patients. During thioproperazine treatment reactions were found excessive and abnormally prolonged. On completion of treatment, when there was no further evidence of autonomic disturbance attributable to the drug, repetition of tests showed no change to epinephrine in those patients whose reading had been normal before treatment, but the rise of systolic blood pressure was increased in those with previously reduced

reactivity. Retested with mecholyl, 50% of the patients showed no change in pretreatment values and the rest exhibited increase and prolongation of reaction. Significantly the latter group showed more marked psychiatric improvement. Other tests were conducted with 5HT, α -methyldopa, and LSD. A return towards normal values was observed and found correlated with psychiatric improvement.

Long Grove Hospital
Epsom, Great Britain

3066 Bigelow, Newton, Ozerengin, Feyzi, Schneider, Jacob, & Sainz, A. Carphenazine in the treatment of chronic schizophrenia. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1102-1105.

Eight-hundred-and-nine patients on carphenazine were studied, using largely the Marcy Psychiatric Rating Scale. The research design excluded immediate and latent placebo reactors. Placebos, mepazine, and fluphenazine groups were used as controls. Carphenazine was found to be specially valuable in chronic schizophrenia and particularly against 1 specific modality named "hypodynamic" where it produced twice as many remissions as fluphenazine and 10 times as many as mepazine. The study of carphenazine aided in isolating this schizophrenic modality. The pharmacology indicates that the principal action is within the cortical and subcortical cerebral cells, with little action on the basal ganglia, hypothalamus and reticular system. Carphenazine induces few and mild extrapyramidal reactions and only scattered hypotensive effects. It does produce a centrocerebral reaction called provisionally an "atypical central nervous system reaction", which appears quite different from the tremulous or dystonic extrapyramidal syndromes usually seen, even with the same drug. The principal side effect of carphenazine is drowsiness and toxic reactions were not observed. Caffeine has been found to be a rapid and effective antidote.

Marcy State Hospital
Marcy, N.Y.

3067 Goldner, Richard D. Control of minor criminal sexual compulsions with imipramine and amine oxidase regulators. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1155-1160.

Forty-seven males were considered in 3 groups: heterosexual, homosexual, and autosexual. Twenty-one exhibitionists were included. Oral medications were prescribed as follows: imipramine 25 mg b.i.d., iproniazid 25 mg t.i.d. or isocarboxazid, 10 mg once or twice daily. Twenty-one were treated with imipramine, 19 with iproniazid, and 7 with isocarboxazid. Twenty-four were markedly improved, 19 moderately improved, 2 slightly improved, and 2 unimproved, with a total of 6 failures who required institutional care. Two deaths from marked cardiac infarction appeared unrelated to therapy.

Saginaw, Mich.

3068 Fox, Richard. Safe sedation? A controlled trial of "Megimated" amylobarbitone. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 966-968.

Twenty mg bemegride (Megimide) did not detract from the hypnotic action of 200 mg amobarbital, nor did it cause any toxic effects in 52 patients (50 completed the trial). Bemegride made little difference, however, in barbiturate hangovers although there was a trend towards lessening them. Four cases surviving large overdosages (10-40 times the normal hypnotic dose) suggests that the mixture may be safer than the use of amobarbital alone.

Bethlem Royal and Maudsley Hospital
Beckenham, Kent
Great Britain

3069 Akimoto, H., Nakakuki, M., Honda, Y., Takahashi, Y., Toyoda, J., Sasaki, K., & Machiyama. Clinical evaluation of the effect of central stimulants, MAO inhibitors, and imipramine in the treatment of affective disorders. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 958-963.

antidepressants were divided into 2 groups: MAO inhibitors and thymoleptics. Pheniprazine, an MAO inhibitor, is effective in the secondary or reactive symptoms of depression such as anxiety, restlessness, and overconcern about minor things. On the other hand, nortriptyline and amitriptyline are effective in the primary symptoms of depression, such as depressive mood and depressive inhibition. Nortriptyline is more effective in simple depression than in the apathetic or neurasthenic types. On the other hand, pheniprazine is more effective in the neurasthenic type, which is often the manifestation of reactive depression. Compared with the ineffectiveness of MAO inhibitors in manic states, nortriptyline proved to be markedly effective.

School of Medicine
University of Tokyo
Tokyo, Japan

3070 Paoli, F., Darcourt, G., & Cossa, P. Sur l'utilisation de l'iminodibenzyl (Tofranil) comme thérapeutique de la douleur. [On the use of iminodibenzyl (Tofranil) as therapy for pain.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 956-958.

Fifty-three patients were treated with nortriptyline (Tofranil) who suffered from various types of pain, e.g., sciatica, pain arising from various cancerous involvements or infection of the urinary tract. Three 5 mg injections were given daily, combined with 12.5 mg levomepromazine or chlorpromazine p.o. at each injection. Results were considered satisfactory in 38 out of the 53 cases. While the mechanism of pain suppression is in doubt, results cannot be obtained by the substitution of placebo.

No address]

3071 Davies, Brian M. Sernyl, its use in psychiatry. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 945-947.

Six patients with longstanding neurotic illnesses were given 3-5 mg phencyclidine (Sernyl) by slow i.v. injection. After treatment patients were asked to write down their experiences under the drug and later these were discussed within a normal psychotherapy interview. Marked ab reactions occurred on 1 or more occasions as significant episodes in the past were remembered. Patients talked little throughout the interview but repetition of words or phrases was common. Feelings of bodily change were often followed by a description of childhood fantasies. One obsessional patient felt that he obtained more benefit from 8 phencyclidine interviews than from 14 previous LSD interviews. Unlike LSD, phencyclidine caused diminution in obsessional rituals for several hours after injection. When the drug became available in oral form, 8 more patients were studied. Five mg were given 1 hour before the interview and then the dose was increased at subsequent interviews to 7.5-10 mg. The drug was helpful in promoting a free flow of emotionally charged material, though in 2 patients the drug produced marked thought bloc, clinically similar to that seen in schizophrenia.

Bethlem Royal and Maudsley Hospitals
Beckenham, Kent
Great Britain

3072 Jean-Yves, & Achallé, Pierre. L'utilisation du R. 381-R. 382 dans les états confusionnels éthyliques ou post-traumatiques, et la désintoxication alcoolique. [The use of R. 381-R. 382 in alcoholic or posttraumatic states of confusion, and in alcoholic cures.] Annales Médico-Psychologiques, 1962, 120, 101-104.

Phenmethazine (R. 381-382) usually in doses of 6 tablets was successful in combating confusional states induced by alcoholism or occurring after traumas. In addition, it was used in connection with standard cures in 100 cases of alcoholism. Whereas formerly, states of confusion appeared with a frequency of 10%, addition of phenmetrazine to the course of treatment prevented the occurrence of such states. Also, its tonic effects counterbalance the lowered tonus and depressive reactions formerly exhibited by some patients.

Centre Psychothérapique,
La Charité-sur-Loire
Nièvre, France

3073 Borenstein, P., Dabbah, M., Blés, G., Roussel, A., & Rosemberger, Mme. Etude clinique de l'éthylbenzotrope (U.K. 738 ou tropéthidryline), correcteur des syndromes extra-pyramidaux dus aux neuroleptiques. [A clinical study of ethylbenzotropin (U.K. 738 or tropethidrylin) an antiparkinsonian agent.] Annales Médico-Psychologiques, 1962, 120, 2, 281-288.

Ethylbenzotropin was administered to 65 patients displaying predominantly extrapyramidal syndromes (excito-tonic seizures and parkinsonism) following treatment with thioproperazine, haloperidol, and other neuroleptics. The drug was administered either orally (2 mg and 5 mg tablets) or i.p. (1 mg or 5 mg ampoules) at doses up to 30 mg. Cure was effected in 53%, and results were excellent in 30%, moderate in 4%, fair in 7% and negative in 7%. Side effects were mydriasis, other visual disorders, dry mouth, asthenia, somnolence and autonomic disturbances. Tolerance was excellent.

Hôpital Psychiatrique
Villejuif, France

3074 Leube, H. Über die Behandlung der Schizophrenie mit einem neuen Psychopharmakon. [The treatment of schizophrenia with a new psychopharmacologic agent.] Therapiewoche, 1962, 16, 688-692.

Fluphenazine was used for the treatment of 95 male schizophrenics, aged 21-73 years. The duration of treatment during hospitalization was 32-168 days; it is strongly recommended that treatment for ambulatory patients be continued for several more weeks or months. The total amount administered during hospitalization ranged from 84-1170 mg; the daily dosage from 3 mg (1 mg t.i.d.) to 12 mg. Fluphenazine was generally administered orally in the form of tablets or drops, in severe cases with psychotic symptoms i.m. (1-3 mg per injection). Of the 95 patients under study, 62 had acute schizophrenia, and 33 chronic schizophrenia. The best results were seen in cases of acute schizophrenia in which symptoms of paranoia and hallucinations were coupled with anxiety and helplessness. The therapeutic effect in chronic schizophrenia was mostly limited to effect on symptoms. It was sometimes necessary to give supporting

medication with a more pronounced sedating effect to patients with catatonic forms of schizophrenia. The rapid onset of action is considered of significant therapeutic value. No toxic or allergic side effects, and no symptoms of somnolence were observed. Extrapyramidal-motor symptoms were seen in 5 out of 95 patients; they could be remedied with administration of antiparkinsonian medication and in most cases without reduction of fluphenazine.

Landesnervenklinik
Andernach/Rhein, Germany

3075 Juenemann, HJ. Erfolge bei der Behandlung von psychosen mit hohen Dosen des benzodiazepin-derivates Librium. [Results in the treatment of psychoses with high doses of the benzodiazepin derivative Librium.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1404-1405.

Four-hundred-and-ten hospitalized patients were treated with chlordiazepoxide (Librium) (average maximal dosage 35 mg-300 mg, in rare instances up to 700 mg daily). The average duration of treatment was 6 1/2 weeks. Of the treated patients 144 were schizophrenic; 92 had various forms of a depression; 49 suffered from epilepsy; 36 had organic brain damage, 36 were psychopaths, 3 suffered from puerperal-psychoses and 50 from miscellaneous diseases. Treatment was successful in 43 (66.15%) of the patients with depression and in 83 (57.64%) of the schizophrenic patients. Anxiety, tensions, irritability, as well as paranoia, motor unrest, agitation, suicidal impulses, guilt feelings, and inhibitions were favorably influenced. Results were restated as follows: 60 very good; 154 good; 49 satisfactory; 132 no effect; 13 condition worse, and 2 uncertain. Tolerance was relatively good. Besides insignificant side effects (sleepiness, slight fluctuations of blood pressure, moderate leucocytosis) there were 43 cases exhibiting somnolence, dizziness, cardiovascular disturbances; 13 cases with conditions of agitation and confusion; 6 cases with neurologic symptoms; 25 cases with disturbances of the autonomic regulation, and 2 cases with allergic reactions.

Pfälzische Nervenklinik
Landeck, Germany

3076 Heinrich, K. Zur symptomprovokation in der therapie der schizophrenie. [The symptom provocation in the therapy of schizophrenia.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C. Third World Congress of Psychiatry Proceedings, Volume II, Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1105-1109.

Symptom provocations in schizophrenia, for diagnostic and therapeutic reasons using MAO inhibitors and imipramine-related drugs [dosage unspecified] is reviewed. Both substances are able to effect emotional mobilization and exacerbation of psychic reactions. Schizophrenic processes and schizophrenic defects seem especially suitable for the symptom provocation. It is not infrequent that, after long-term ineffective therapy with neuroleptic agents or intense shock therapy, activation of the psychosis finally provides the 1st step to improvement. These observations are supported by Deschamps who stated that schizophrenic psychoses that do not react with increase of symptoms after administration of mescaline have a poor prognosis.

Universitäts-Nervenlinik Mainz
Mainz, Germany

3077 Gerstenbrand, F., & Pateisky, K. Über die Wirkung von L-Dopa auf die motorischen Störungen beim Parkinson-Syndrom. [The effect of L-DOPA on the motor disturbances of the Parkinson-syndrome.] Wiener Zeitschrift für Nervenheilkunde und deren Grenzgebiete, 1962, 10, 90-100.

In agreement with results obtained by other investigators, clinical observation and extensive electromyographic investigations have shown that the effect of L-DOPA on Parkinson's syndrome of the postencephalitic patient is intensified after pretreatment with MAO inhibitors (100 mg DOPA in 200 cc saline iv, after 5 days of 10 mg isocarboxazid t.i.d., p.o.). The most significant effect was that on akinesia and rigor, less evident than on tremor at rest, while action tremor was not influenced at all. The improvement was objectively still evident after 24 hours;

subjectively even after 3-5 days. Side effects were not observed.

Psychiatrische-Neurologische Universität
Vienna, Austria

3078 Schwarz, H. Therapeutische Erfahrungen mit Nialamid. [Therapeutic experiences with nialamide.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II, Toronto/Montreal: University of Toronto Press, 1962. Pp. 1405-1406.

Two separate investigations using nialamide were carried out. In the first study, 174 patients were treated for an average of 40 days (1-3 tablets t.i.d.). The patients were suffering from depressions of various genesis, as well as from epilepsy and schizophrenia. Good therapeutic results were seen in endogenous and involuntal depressions and less favorable results in schizophrenia. The tolerance was good. In the second double-blind study, 157 patients were treated for a period of 2-3 months. Good results were seen in 68 patients; 67.3% of these were seen in psychopathic patients, and in those suffering from epilepsy, depressions during aging, and endogenous and symptomatic depression. Good results were seen in patients with arteriosclerotic dementia, imbecility, atrophic brain processes, and schizophrenia (40-50%). Of 36 cases in the placebo group 9 appeared improved, though 4 of these patients had received additional medication. Fifty-three patients showed no change. The following results with regard to dosage were observed: of 42 patients which had received 50 to 150 mg daily, 69.2% showed good results; of 46 patients with an average dosage of 100-300 mg, 56.3% good results; of 33 patients with an average daily dosage of 150-450 mg, 40% good results. Best results may be achieved with 100-200 mg/day, while higher doses might be necessary for individual cases but may lead to increased agitation. Administration of higher dosages did not speed up onset of effect.

Pfälzische Nervenlinik,
Landeck über Landeau/Pfalz
Germany

3079 Tweedy, P.S. A clinical trial of heptabarbital (Medomin). *Gerontologia Clinica*, 1962, 4, 276-280.

A double-blind trial was used in which 0.2 g butobarbital (2 tablets) were compared with 0.4 g (2 tablets) of heptabarbital (Medomin). Each patient tested was given the drugs on successive nights or on the 1st and 3rd nights without any sedative on the intervening night. With 31 patients, 60-90 years of age, no difference was found between them in regard to effectiveness of sedation; the incidence of confusional states was much the same for both.

St. Thomas' Hospital
Stockport, Cheshire
Great Britain

3080 Wittenborn, J.R., Plante, Marc, Burgess, Frances, and Maurer, Helen. A comparison of imipramine, electro convulsive therapy and placebo in the treatment of depressions. *Journal of Nervous and Mental Diseases*, 1962, 135, 131-137.

The efficacy of imipramine, ECT and a placebo was compared in the treatment of newly-admitted, female depressives. None of the patients appeared to be schizophrenic or addicts. The placebo and imipramine were indistinguishable and the dosage (which did not exceed 200 mg/day) was determined by the physician in charge of the patient. Assignment of patient to treatment groups was pre-determined on a random basis: Patients were observed, tested, and rated before assignment to groups, when they were ready to go home, or at end of ten weeks. Tests and ratings represented criteria for the major characteristics of depression. Using the method of analysis of covariance, an adjustment post-treatment mean for each treatment group was found, and comparison of these means indicated the relative efficacy of the treatment. The imipramine group was found to be superior to the placebo group with respect to symptoms of anxiety and depression, subjective depression as revealed by the MMPI, and the "friendly" score on the Clyde Mood Scale. The imipramine group showed a much shorter latency than the ECT group on the Standard Interview. The ECT group was superior to the placebo group with respect to the

subjective aspects of depression as measured by the psychasthenia and depression scores on the MMPI and the "friendly" score on the Clyde Mood Scale. Imipramine may be more generally efficacious than ECT in the sense that its ameliorating effects appear to influence more aspects of behavior than does ECT.

Rutgers University Interdisciplinary
Research Center
New Brunswick, N.J.

3081 Flach, Frederic F., Burrell, Craig D., & Liang, Edward. Alterations in calcium metabolism in depressed patients receiving imipramine. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1409-1414.*

Imipramine (150 mg/day p.o. for 4-6 weeks and occasionally longer) was administered to 12 psychiatric patients maintained on constant medium calcium diets (800 mg/day). Six patients showed alleviation of depression with a reduction in urinary calcium excretion. One patient demonstrated fluctuations in depression, associated with corresponding fluctuations in urinary calcium and phosphorus. Five patients failed to demonstrate significant clinical or metabolic changes during imipramine therapy. The impression is strengthened that changes in calcium metabolism or in factors influencing calcium may contribute to the development or persistence of certain depressed states.

Payne Whitney Psychiatric Clinic
525 East 68 St.
New York 21, N.Y.

3082 Torrico, August. Administracion por via intraraquidea de algunos medicamentos en enfermedades mentales. [The intraspinal administration of some drugs to mental patients.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 968-973.*

Seventy-eight patients in states of agitation (oligophrenia, alcoholism, manic depressive psychosis manic type, acute and chronic schizophrenia, and epilepsy) were given 2.5-7.5 mg

reserpine as a single injection intraspinally every 24 hours. Usually 2 injections were given. Sixty-two of the cases were successfully sedated. The 16 cases which were treated unsuccessfully were: 12 manic depressive psychosis, 3 oligophrenia and 1 alcoholism. Headache was the most frequent side effect. Additionally, 52 schizophrenics (22 chronic cases and 30 acute) were treated with twice weekly intraspinal injections of 2.5-5 mg reserpine. Treatment lasted 2-10 months. Results were good, and were considered best for acute cases. In 6 cases no modification was obtained. Further, 64 epileptics were given similar treatment and the number of convulsions was notably reduced. The diuretic, acetazolamide, and the psychoactive drug, perphenazine, were also used adjunctively intraspinally. Acetazolamide caused no substantial modification in the EEG of epileptics.

Hospital Psiquiatrico
Universidad de Chile
Santiago, Chile

3083 Henne, M. Michel, Henne, Suzanne, Kogi, M. Sadataka, & Tonnel, Micheline. Cinq années de recul dans l'emploi personnel de la levomépromazine (7044 RP, Nozinan) chez 500 hospitalisés. [Five years personal use of levomépromazine (RP 7044, Nozinan) in 500 hospitalized patients.] In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962 Pp. 976-979.

Levomepromazine, devoid of serious and dangerous side effects, is more efficacious than chlorpromazine in agitation, particularly acute manic excitation. It has been used for over 5 years in 500 hospitalized patients suffering from various psychoses. It is less active against hallucinations than chlorpromazine but particularly potent in the control of anxiety and insomnia. It is effective against suicidal melancholia and allows a reduction in the number of ECT needed. The dosage varies between 100-1000 mg for adults and 25-400 mg for children over 5 years of age. Somnolence and slight arterial hypotension at the beginning of the treatment is usual. Prolonged use can lead

to extrapyramidal reaction, amenable to antiparkinsonian drugs and the combination to psychotonics. No mortality has been observed in spite of massive ingestion by patients attempting suicide.

Hôpital de Saint-Venant
Saint-Venant, France

3084 Lindsley, Ogden R. Direct measurement and functional definition of vocal hallucinatory symptoms in chronic psychosis. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 983-986.

Chlordiazepoxide was considered the most effective drug currently available in the treatment of tension and/or anxiety states. Over 30 thousand hours of data were collected from 80 adult chronic psychotics. Patients sat in a small 6 x 6 foot experimental room containing a chair on 1 wall, a small plunger, and delivery tray. The operation of this plunger (a free operant response) could be made to deliver automatically various reinforcers to the patient on different schedules of intermittent reinforcement. The nature of these reinforcing events, (e.g., food, candy, money) determines the class of motivation that is being investigated. The different rates of plunger responses are recorded on cumulative response recorders and indicate the patient's current interest in and ability to work for different reinforcers. Both manual non-sympathetic responses and vocal sympathetic responses of overtly hallucinating patients were directly and simultaneously recorded. Vocal hallucinatory symptoms, and possibly all psychotic symptoms, are defined in terms of their functional rather than topographical or bizarre properties. Vocal symptoms appeared to have the following functional properties: (1) an abnormally high degree of nonmechanical competition with strongly reinforced nonsymptomatic behavior; (2) the ability to be elicited by hidden stimuli of incomplete topography in the appropriate modality; (3) an abnormally long after-discharge from such elicitation, and (4) independence of their environmental consequences or direct reinforcement.

Harvard Medical School
Boston, Mass

3085 Mall, G. Some observations on the aetiology and therapy of endogenous depressions. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1402-1404.

The treatment of periodic depressions (post-menstrual period or in the puerperium, i.e., women 22-38 years of age; 35 patients) with estradiol combined with testosterone [dosage unspecified] resulted in radical fading of the depressions; phenothiazines, meprobamate, and imipramine were not particularly effective when not supported by hormone therapy. Depot-testosterone treatment of male psychotic depressives with 250-500 mg/ month and in obstinate cases in combination with chorionadotropin (24-40,000 μ /month) results frequently but not always in a satisfactory remission. The short term use of ACTH and the use of deoxycorticosterone with antidepressants such as chlorthalidoxepoxide and MAO inhibitors like isocarboxazid, opium, or haloperidol was also discussed. Depressions in women in menopause and old age, have responded to depot-testosterone (250 mg/month) combined with 3 mg estradiol.

Pfälzische, Nervenlinik
Landeck über Landau/Pfalz
Germany

3086 Billig, Otto, & Adams, Robert W., Jr. Middle-age depressions. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1406-1409.

In a series of 100 consecutive patients seen for psychiatric evaluation in connection with application for total and permanent disability, 90 patients fell into the 40-60 age group. Most of the claims were initially on physical disability; psychiatric evaluation was obtained when physical symptoms appeared largely functional. Sixty-four out of 90 patients were males. The diagnosis of chronic anxiety was made in 18 males and 19 females. The next diagnostic group was organic brain syndrome with cerebral arteriosclerosis (15 males). Ten patients were schizophrenic and 5 were diagnosed as manic

depressive. Three males were diagnosed as having depressive reaction and a variety of neurotic, psychotic and personality disorders made up the remainder. Depressions of an earlier age respond more promptly to therapy than those of middle age. Poor results were obtained with imipramine or MAO inhibitors, as well as ECT.

614 Medical Arts Bldg.
Nashville 12, Tenn.

3087 Sainz, Anthony, & Bigelow, Newton. Relative antidepressant activity of various chemical groups. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings, Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1387-1393.

During the clinical evaluation of chlorphenoxamine, isocarboxazid, tranlycypromine, imipramine, and amitriptyline, then caffeine, pentetrazol, methylphenidate and dexamphetamine, as well as chlorpromazine, thioridazine and fluphenazine in endogenous and exogenous depressive inpatients, biochemical determinations of catecholamines, 5HT, tryptamine, dopamine and tyramine excretory levels were as yet made. An unidentified group of aromatic amines that fluoresce in the vicinity of tryptamine (265-286 $m\mu$) called "x-neuramines" was noticed. The best therapeutic results were obtained with the hydrazine-type MAO inhibitors. Alloxazine derivatives are also recommended for "larval depressions," neither group of drugs is particularly suitable in dealing with endogenous depression in the older age groups. Analeptics have no value in either type of depression and may be harmful. Chlorphenoxamine and isocarboxazid have the highest antidepressant effect, and amitriptyline ranks next, ahead of imipramine which follows; tranlycypromine shows up as quite a weak drug. Therapeutic efficacy appears limited only by toxic thresholds. Effective antidepressants appear to achieve their results through neuramine potentiation at the cerebral level.

Marcy State Hospital
Marcy, N.Y.

3088 Degkwitz, Rudolf. The effect of imipramine (Tofranil) in different kinds of depressions in comparison with electro-shock treatment - a report on 600 cases. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 1394-1395.

Imipramine alone, with a tranquilizer, or ECT was used in the treatment of 120 depressives (496 inpatients and 113 outpatients); 86% of the patients, mostly women, improved within the 1st 22 days of treatment and almost the same percentage had side effects during this time. Best results were obtained when imipramine was continued in dosages of 200-250 mg/day. When it was increased to 300-350 mg/day and then reduced to about 100-105 mg/day, results were less satisfactory. A dose of 100-150 mg/day apparently leads to the poorest result, but in combination with a tranquilizer almost the same percentage of good responses was obtained. With outpatients only small doses were used because of complaints of side effects; poor results were obtained with imipramine only. Combined treatment (addition of thioridazine) proved much more successful. ECT results were superior (70-80% improvement) to results obtained with imipramine, however imipramine-treated patients spend 25% less time in the hospital than the ECT patients. The combination of imipramine with ECT does not seem to improve results obtained with imipramine alone (based on 25 patients).

Heinrich Hoffman Str. 12
Frankfort/Niederrad, Germany

3089 Grosser, George H., & Freeman, Harry. Differential recovery patterns in the treatment of acute depression. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1396-1402.

One-hundred patients, 24 men and 76 women, suffering from acute depression were each assigned to 1 of 4 treatment modalities in a double-blind, randomized study. Three drug groups were compared to an ECT group. The drugs and dosages were isocarboxazid, maximal obligatory dose 40 mg with another

10 mg optional; phenelzine maximal 60 mg with another 15 mg optional; imipramine, minimal 150 mg with another 37.5 mg optional. Dosages reached maximal in the 3rd week of treatment. ECT, modified by suxamethonium, was given with a minimal of 9 treatments (3 weekly for 3 weeks) with further treatments based on clinical judgment. The full treatment period for all was limited to 8 weeks, though patients could be discharged at any time after 4 weeks of treatment. Psychoneurotic depressive reactions show marked improvement and no failures, whereas patients in the psychotic groups show 25-50% treatment failures. While all treatments work well for psychoneurotic depressive reaction, ECT proves somewhat more effective in affective psychoses. MAO inhibitors show a more gradual response in the 1st 3 weeks than ECT and imipramine, but the improvement rate remains steadier throughout the 8-week period. ECT and imipramine show maximal change in the first 3 weeks, with subsequent slowing in improvement rate.

Mental Health Center
74 Fernwood Road
Boston, Mass.

3090 DeVerbizier, J., Guillon, A., & Benkhoucha, M. A propos de cures d'amaigrissement par le 8.228 R.P. en milieu hospitalier psychiatrique. [Antiobesity treatment with RP 8-228 in a psychiatric hospital environment.] Toulouse Médical, 1961, 63, 437-443.

Eighteen paranoid patients (16 women and 2 men), were treated for overweight with levophacetoperane (5 and 20 mg tablets, 20-120 mg/day, usually in 3 doses an hour before meals). Treatment lasted about 5 months, with a range of 1-19 months. The agent had a clear anorexic effect in 11 cases, moderate action in 2 cases and no appetite suppressing effect in 5 cases. One bedridden woman was able to go back to normal routines in the hospital after a weight loss of 26 kilos. Tolerance was excellent and side effects occurred in only 2 cases: epigastric cramps in 1 and generalized fatigue in the other.

Société de Neurologie et Psychiatrie
de Toulouse et du Sud-Ouest
Toulouse, France

3091 Gayral, L. Resultat de cent traitements par imipramine (Tofranil). [The result of 100 treatments with imipramine (Tofranil)] Toulouse Médical, 1961, 63, 435-437.

One-hundred patients suffering from anxiety-melancholia were treated with 100-250 mg/day imipramine, p.o. or i.m. Twenty-six percent were cured, 29% showed no change, 25% were found intolerant necessitating the cessation of medication, 17% improved temporarily, and 3% showed improvement but also intolerance necessitating discontinuation of imipramine. Side effects were as follows: 1 case of polyneuritis, 3 erythrodermic eruption, 2 confusion, 5 excitation and insomnia, 1 ataxia with trembling and anxiety, 2 stupor and 9 cases of gastrointestinal upset with autonomic disturbances, nausea and hypotension. Results could be restated as 33% good, 33% poor, and 33% intolerance.

[No address]

3092. Chanoit, P., & Vallée, A. L'emploi de la thioridazine en psychiatrie. Réflexions critiques d'une expérience clinique. [Thioridazine in psychiatry. Critical reflections on clinical experience.] Annales Médico-Psychologiques, 1962, 120, 104-109.

Thioridazine was administered in tablet form to 55 patients, in doses of 50-300 mg per day. Good results were obtained in 24 cases, moderately good in 14, poor results in 7, no effect in 8, and aggravation in 2. Persons under 60 responded to treatment better than the older patients. Better results were obtained in acute than in chronic conditions. The drug is principally indicated in anxiety, depression, schizophrenia, chronic deliriums, and alcoholic neuroses. Thioridazine was extremely well tolerated and very simple to administer.

[No address]

3093 Mellien, G. Klinische Erfahrungen mit Tryptizol. [Clinical experience with Tryptizol (amitriptyline).] Therapiewoche, 1962, 22, 999-1003.

Amitriptyline was used in the treatment of 58 hospitalized patients, aged 18 to 72, suffering from severe depressions of various

genesis (75-200 mg p.o. or 5-10 cc i.m., b.i.d.). The treatment was continued for 3 to 4 weeks. The patients were kept in bed until a marked therapeutic effect became evident, which occurred in most cases on the 3rd to 7th day. The results of the treatment were classified as follows: 0-effect; improved (I); to be discharged (D). The following results were obtained: Melancholia 13 (D), 1 (0-effect). Climacteric depression: 6 (D), 2 (0-effect); depressions due to organic brain diseases 5 (D), 5 (I), 4 (0-effect); reactive depressions 4 (D), 1 (I), 2 (0-effect); depression in schizophrenics: 6 (D), 1 (I), 8 (0-effect). The tolerance of amitriptyline is considered excellent. Dryness of the mouth was observed in 30% of all cases. Slight temporary drop in blood pressure was frequently observed. Clinical observation and laboratory investigations did not show damage to bone marrow, liver, or kidneys.

Westfälische Landeskrankhaus für
Psychiatrie
Warstein, Germany

3094 Lichstein, Jacob, & Mayer, Jay De Costa. Symptoms of autonomic imbalance and treatment in gastro-intestinal dysfunction. American Practitioner, 1962, 13, 303-306.

Chronic gastrointestinal dysfunctions are a large area of psychosomatic problems involving the use of tranquilizers. Twenty-three cases of gastro-intestinal dysfunction with autonomic nervous system disturbances were treated with placebo, thioridazine, and an autonomic stabilizer (Bellergal; 0.6 mg ergotamine, 0.2 mg bellafolline, and 40 mg phenobarbital. Thioridazine dosage was 10 mg t.i.d., and Bellergal was administered t.i.d., as was placebo for periods of 2 weeks each. The autonomic stabilizer has the highest incidence of overall improvement, i.e., 61% followed by thioridazine with 48% and placebo with 34%. The 2 symptoms which appear to improve most consistently with the stabilizer were constipation and diarrhea. No side effects were encountered with thioridazine. Apparently, thioridazine is not useful in anxiety states manifested chiefly by dysfunctional gastrointestinal symptoms.

University of Southern California
School of Medicine
Los Angeles, Calif.

3095 Bartholomew, Allen A., & Bruce, David W. The modification of a side effect (drowsiness) of chlordiazepoxide ("Librium") by amiphenazole: preliminary communication. Medical Journal of Australia, 1962, 149, 927-928.

A double-blind trial using 20 mg chlordiazepoxide, 200 mg amiphenazole, and 20 mg chlordiazepoxide plus 200 amiphenazole was conducted with 36 outpatients. Patients fell into 3 crude diagnostic categories: remitted alcoholics (15), mixed neurotics (11) and character disorders or psychopathic personality (10). The dose was 1 tablet t.i.d. and the duration of the trial up to 6 weeks. If clearcut drowsiness was observed, the regimen would be stopped for the individual and more orthodox therapy initiated. Drowsiness was experienced by 12 patients, 7 on chlordiazepoxide, 2 on amiphenazole, and 3 on the combination. The trial did not remain on a true double-blind basis, because it was apparent before the end of the trial that obvious drowsiness was more likely due to chlordiazepoxide.

Alexandra Clinic
Melbourne, Australia

3096 Van Rhijn, C.H. An evaluation of Melleril by means of a controlled group. Psychiatria, Neurologia, Neurochirurgia, 1962, 65, 117-128.

Thioridazine (Melleril; 150-900 mg/day) was administered to 50 patients (22 chronic schizophrenics, 15 schizoid psychosis, and 13 miscellaneous) for 6-12 months. Results were best in patients with paranoid reactions. Of the 22 schizophrenics, 11 improved notably, as did 12 out of the 15 schizoids. Minimal side effects included tiredness, sleepiness, inactivity, restlessness, vomiting, etc.

Mental Hospital "Brinkneven"
Deventer, The Netherlands

3097 Wilson, W.P., Johnson, J.E., & Smith, R.B. Affective change in thyrotoxicosis and experimental hypermetabolism. Progress in Neurology and Psychiatry, 1962, 17, 234-246. [Discussion]

Complete medical and psychiatric examinations were performed on 26 hyperthyroid patients. The Clyde Mood Scale was administered to 16 of them. Large doses of triiodothyronine (300 µg/day for 3 days) were administered to 11 normal subjects and changes in affect were determined according to the Clyde Mood Scale. The predominant symptomatology of thyrotoxic patients is affectively determined and the presence or absence of symptoms correlates well with Clyde Mood Scale scores. The administration of thyroid hormone produced depression, decreases friendliness, and increases jitteriness in normal subjects.

[No address]

3098 Bartholomew, Allen A. An evaluation of tranlycypromine ("Parnate") in the treatment of depression. Medical Journal of Australia, 1962, 149, 655-661.

A double-blind study of tranlycypromine was made of 84 depressive outpatients (6-week trial). The initial dose was 10 mg t.i.d.; it was doubled after 2 weeks if neither patient of a pair showed any improvement. Side effects were mild and those causing cessation of treatment were hypomania (if it may be called a side effect), dependent edema, impotence, nausea and vomiting. Global results showed tranlycypromine superior to placebo. However tranlycypromine did not significantly differ from placebo in either endogenous or involutional depression. In the case of reactive depression the drug was superior. Improvement, when it occurs, should be evident after about 2 weeks of treatment.

Alexandra Clinic
Department of Mental Hygiene
Victoria, Australia

3099 Richardeau, N., & Asfar, M. Spasmes de la face et du cou a caractère extrapyramidal après 36 ans d'évolution d'une psychose périodique. Action thérapeutique contre les spasmes du majeptil. (Presentation de malades). [Spasms of the face and neck, extrapyramidal in character, after a 36 year period of recurrent psychosis. Therapeutic action of thioproperazine (Majeptil) against spasms. (A case history).] Annales Médico-Psychologique, 1962, no. 1, 71-77.

A 66-year-old woman, who had suffered from encephalitis 36 years previously and had been under treatment for 35 years for a recurrent psychosis of a marked agitational type, suddenly developed uncoordinated spasms, primarily of the face and the neck which also affected the general musculature. Extrapyrarnidal hypertonia, due to chlorpromazine administration, was believed the cause. Treatment with thioproperazine, in doses of 15 mg twice weekly, for several months suppressed extrapyramidal manifestations. Cessation of thioproperazine therapy was followed by reappearance of symptoms.

Service du Professeur Baruk
Saint-Maurice (Seine),
Paris, France

3100 Sila, Basri, Mowrer, Marie, Ulett, George, & Johnson, Margaret. The differentiation of psychiatric patients by EEG changes after sodium pentothal. *Progress in Neurology and Psychiatry*, 1962, 17, 191-199; discussion 199-203.

Thirty-nine schizophrenics and 19 psychotic depressive cases were studied before and after thiopental (Pentothal). After 5 minutes of resting EEG recording, 100 mg thiopental was injected i.v. in 5-7 seconds. The drug was reinjected twice more at 2-minute intervals, giving a total of 300 mg in a 4-minute period. Patients were observed until EEG tracings returned to pre-medication levels. Both groups of mental patients had similar basic resting EEG's. Thiopental produced an increase in EEG activity frequencies, particularly in the β range. There was a significant difference in the reaction of the 2 groups with a quantitatively greater EEG response in the schizophrenic subjects. When a group of 24 patients was carefully selected from a larger group and dichotomized on the basis of symptoms typical for schizophrenia or depression, and with little or no overlapping, no significant difference in response between the 2 groups of patients was found. In the discussion Goldman reviews thiopental-activation studies in about 2,000 patients.

[No address]

3101 Gould, Arnold H. Combined dextbrompheniramine-fluphenazine (Diperm chronotab) in the oral treatment of pruritis. *Journal of New Drugs*, 1962, 3, 179-182.

The combination of an antihistaminic and a tranquilizer, Diperm Chronotab (6 mg dextbrompheniramine and 2.5 mg fluphenazine; 3 tablets daily) was used in the treatment of 97 cases of pruritis. The reference drug used was a sustained-release capsule of 5 mg trimeprazine in crossover trials which were conducted with 47 patients and the remaining studied in double-blind trials. Mild drowsiness occurred in about 10% with either drug or reference drug. Complete or marked relief of itching was noted in 85% with Diperm and 59% with trimeprazine. Diperm b.i.d. appears effective for the oral treatment of itching.

Department of Medicine
Georgetown University School of Medicine
Washington, D.C.

3102 McDonald, Robert L., & Gynther, Malcolm D. Effects of verbal stimuli on autonomic responsivity of medicated and non-medicated schizophrenics and character disorders. *Journal of General Psychology*, 1962, 66, 287-299.

Thirty-six male patients, 18 schizophrenics and 18 character disorders, aged 16-44 years, 1st admissions except for 3, were tested for autonomic responsivity, i.e., heart rate, galvanic skin response reactivity and recovery time, and respiratory reactivity under emotion-provoking stimulus conditions. Three groups were established: meprobamate, prochlorperazine, and non-medicated. The medicated patients received standard dosages (10 mg prochlorperazine t.i.d. and 400 mg meprobamate t.i.d.) for a period of 3-4 days prior to testing. The stimuli, which consisted of 12 incomplete sentences, were selected to tap conflict areas of schizophrenic and character disorder patients. Five of these were devised and 7 sentences were chosen from the Sacks sentence completion test. Prochlorperazine tends to reduce the galvanic skin response reactivity and recovery time in schizophrenics, but increase the factors in character disorder cases. Meprobamate tends to increase autonomic nervous system activities in both schizophrenics and character disorder cases. There are no significant differences between these 2 groups for any of the autonomic measures. Heart rate and respiratory reactivity were

relatively unaffected by either drug, and the stimuli generally did not elicit differential psychological responsivity presumably associated with mother-relations, guilt-feelings, authority -figures and the early family constellation.

Department of Psychiatry
South Carolina State Hospital
Charleston, S.C.

3103 Horne, E. Porter, & Deabler, Herdis L. Optimal beta motion in patients receiving insulin and chlorpromazine treatment. *Journal of General Psychology*, 1962, 67, 265-269.

The behavior of 94 psychiatric patients and 12 normal subjects in a narrow visual field stimulated by an apparatus capable of producing optimal beta motion was studied. Twenty-three of the subjects showed good recovery from insulin treatment. Ten others were used in the immediate recovery phase following insulin coma treatment. Eighty-two patients received 100-800 mg chlorpromazine daily. Twenty-nine organic patients were included. Beta motion was perceived readily at a fast rate by normal subjects while patients on insulin treatment at least temporarily reported a higher sensitivity to motion perception. The effect of chlorpromazine was in the direction of a lowered beta motion perception and was more like the perception found in organic patients than in normals.

University of Florida and Gulfport
Division
VA Center
Biloxi, Miss.

3104 Karras, Athan. The effects of reinforcement and arousal on the psychomotor performance of chronic schizophrenics. *Journal of Abnormal and Social Psychology*, 1962, 65, 104-111.

Eighty male chronic schizophrenics performed a visual 2-choice RT task. All subjects were on tranquilizers. The subject made a jump reaction from the rest button to a telegraph key under which the response light was illuminated. During the experimental condition, subjects responded under 1 of the following treatments: medium or

high stimulation, in which an auditory stimulus was presented constantly; low or high escape in which an auditory stimulus was presented from which the subject could escape, and control, which had no such collateral stimulus. The control and low escape groups performed the same. The high escape group performed better than the control group, and the 2 stimulation groups did worse than the control. For the post-experimental condition, the medium stimulation of the low escape group was found worse than the others which were not different from each other. Improvement in the psychomotor performance of chronic schizophrenics presented with an intense stimulus characterized as aversive was a function of reinforcement rather than solely as an increase in the level of arousal.

University of Rochester
Rochester, N.Y.

3105 Bennett, Ivan F. The constellation of depression: its treatment with nortriptyline. II. Clinical evaluation of nortriptyline. *Journal of Nervous and Mental Disease*, 1962, 135, 59-68.

Nortriptyline was proven a safe and effective antidepressant in a trial with 75 patients represented by both outpatients and hospitalized groups and including psychotic, psychoneurotic, geriatric, neurologic and psychosomatic cases. Side effects were few and mild, e.g., 16% dry mouth, 16% drowsiness, 12% increased psychomotor activity and 12% dizziness. Dosage was 25 mg nortriptyline b.i.d. to q.i.d. Global clinical improvement was 37%. In relation to target symptoms, improvement was 82% for depression, 70% for hostility and 74% for anxiety.

Lilly Laboratory for Clinical Research
Marion County General Hospital
Indianapolis, Ind.

3106 Gradillas Regodon, Vicente. Observaciones sobre el tratamiento de esquizofrenicos cronicos con fluorclorpromacina. [Observations on the treatment of chronic schizophrenics with trifluorpromazine.] *Medicina*, 1962, 30, 97-99.

A double-blind study was conducted with 50 chronic schizophrenics, hospitalized for over 10 years, 25 on trifluorpromazine and 25 on placebo. Trifluorpromazine dosage was 200 mg/day for 3 months. Side effects consisted of edema,

anorexia, hypokinesia, trembling, unrest, rapidly alleviated with promazine injections. Some improvement especially in relation to deliriums or hallucinations was obtained, without real effect on the schizophrenic disease process. A practical rule is to begin with a drug such as chlorpromazine or reserpine, and if favorable results are not obtained to switch to another product.

Hospital Psiquiatrico de Leganes
Leganes, Spain

3107 Rondepierre, J.J., Ropert, R., & Azoulay, J. Sur l'utilisation clinique en neuro-psychiatrie du chlorhydrate d'éthyl-3-(méthyl-2'-diméthylamino-3'-propyl) 10 phénothiazine (6484 RP) nouveau neuroleptique phénothiazinique. [On the clinical employment in neuro-psychiatry of ethyl-3-(methyl-2'-dimethyl-amino-3'-propyl) 10 phenothiazine HCl (RP 6484), a new phenothiazine neuroleptic.] Presse Medicale, 1962, 70, 1342-1344.

Ethotrimeprazine was administered to 42 hospitalized and 26 ambulatory patients, suffering from delirious psychoses, schizophrenia, melancholia, depression, etc., at 40-400 mg doses for the hospitalized group, and 20-100 for ambulatory patients. Neuroleptic effects obtained were similar to those of chlorpromazine or levomepromazine, while the side effects noted with the latter drug were absent. Tolerance was excellent. The drug does not have any inherent antidepressant action, and its combination with imipramine results in synergistic action.

[No address]

3108 Priest, R.G., & Forrest, A.C. Nethalide. The Lancet, 1962, No. 7253, 451.

No direct evidence of psychopharmacological effect for nethalide has been established. A 200 mg single oral dose was given to 5 normal volunteers who reported: 2 no effects, 1 fatigue, and 2 noted giddiness. One female depressed patient was given 200 mg t.i.d. for 7 days with no effect. This patient later improved with 15 mg phenelzine t.i.d. A manic depressive female in a depressive phase was given 50 mg nethalide i.v. with no effect; the same was true for a schizophrenic

female. Four other chronic schizophrenic females showed no improvement on 300 mg nethalide t.i.d. Nethalide had no effect when given previous to methamphetamine. Finally 2 staff members took 2.5 mg dexamphetamine and 200 mg nethalide; here nethalide showed no activity.

Royal Edinburgh Hospital
Morningside
Edinburgh, Great Britain

3109 Gratton, L., Houde, L., Lafontaine, R., & Fournier, G. Syndromes hypermoteurs et trifluoperazine. [Hypermotor syndromes and trifluoperazine.] Canadian Psychiatric Association Journal, 1962, 6, 257-260.

Thirty-three children, 7-12 years old, suffering with hypermotor syndrome were separated into 3 groups of 11 each, on the basis of comparable pathological psychic conditions. Each child was given either trifluoperazine (0.5 mg/10 lb) or placebo, or remained without medication. Motor hyperactivity declined in the group of children under trifluoperazine with normal neurology, whose hyperactivity was the expression of emotional disturbances, and rose in that group of children in whom hyperactivity was the expression of extrapyramidal syndrome, frequently accompanied by muscular hypertonia, etc. In the 3rd group the reactions were mixed.

Service de Psychiatrie Infantile
Hôpital Ste.-Justine
Montreal, Quebec
Canada

3110 Horne, P.M., & Forrest, A.D. Pilot trial of I.C.I. 31397. A new mono-amine oxidase inhibitor. Scottish Medical Journal, 1962, 1, 224-229.

I.C.I. 31397, α -methylbenzylhydrazine, was administered to 24 patients: 8 chronic hospitalized depressives, 9 recently admitted depressives and 7 outpatients with mild or depressive illnesses. Dosage was 3-20 mg/day and the conclusion reached that optimal therapeutic range was 15-30 mg/day. At 2 weeks, 62.5% showed improvement. Two patients showed abnormal cephalin cholesterol flocculation test and possibilities that hepatotoxicity should be further investigated.

Royal Edinburgh Hospital for Mental Disorders
Edinburgh, Great Britain

3111 LaVeck, Gerald D., de la Cruz, Felix, & Thomas, David B. Anticonvulsant properties of amino-oxyacetic acid: clinical studies. *Journal of New Drugs*, 1962, 2, 160-166.

Eight patients were treated with a standard oral dosage of 50 mg aminooxyacetic acid q.i.d. for 4 months. EEG's were obtained before and after. Some dosage reductions were necessitated by drowsiness. As this pilot study indicated that aminooxyacetic acid had anticonvulsant properties, a double-blind study with 30 mentally retarded patients with epilepsy and organic brain damage was begun. The agent was started at 25 q.i.d. and increased 2 weeks later to 50 mg q.i.d. except for the 2 youngest patients, i.e., here maximal dosage was 100 mg/day. Side effects occurred in 2, severe drowsiness and abnormal liver function tests, but both were in the placebo group. In the double-blind study no difference was exhibited between drug and placebo.

Rainier School
Buckley, Washington

3112 Angst, J. Tofranil: a clinical analysis. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress of Psychiatry Proceedings*. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1383-1387.

Two hundred depressive patients, including 137 patients suffering from endogenous depression, were treated with imipramine (Tofranil) over a period of 1½ years. In endogenous depression, imipramine proved effective in 2/3 of the cases to the extent that patients were able to resume their place in society with 16% symptom-free. Follow-up studies over 12 months show that a completed course of imipramine therapy does not reduce the risk of relapse. Forty-nine patients had been previously treated with a dose of ECT, remission being achieved in 2/3. Forty-seven percent responded favorably to both forms of treatment, 23 to ECT, 20% to imipramine only, and 10% remained completely refractive to both forms of therapy. Usually treatment trials on relative suffering from different endogenous psychoses (including schizophrenia) indicated that a close similarity in response to imipramine is demonstrable only within the clinical entity

designated as endogenous depression. This appears to concern the value of classical psychiatric nosology and indicates that investigations into the affects of the drug among adult relatives opens up new possibilities for clinical research.

Psychiatrische Universitätsklinik
Burgholzli, Zurich
Switzerland

3113 Busfield, Bernard L., Jr., Wechsler, Henry, & Barnum, William J. A physiological correlate of diagnosis and treatment outcome in depression. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress of Psychiatry Proceedings*. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1367-1371.

One-hundred nine severely depressed adult in-patients in three different hospitals were treated for a 4-8 week period with either isocarboxazid (20 mg/day, up to 50 mg/day), chlorphenoxamine (30 mg/day), imipramine (75 mg/day, increased to 185 mg/day) or ECT (3 treatments/week for a minimum of 3 weeks). After selection, each patient underwent a 5-day pretreatment clinical assessment which included determination of salivation rate by the Peck technique. Perceptual complaint of dry mouth, diagnosis, assessment of severity of depression, and determination of improvement were carried out independently of salivation collection by different psychiatrists. Patients with reactive (endogenous) depression had significantly higher rates of salivation compared with those with nonreactive (endogenous) depression, including involutional and manic-depressive cases. Female depressed (more often endogenous in diagnosis) salivate at significantly lower rates than male counterparts. Salivation rates do not vary with severity of depression in any diagnostic groups. There is no correlation of perception of dry mouth with diagnostic category, nor actual measured physiological hyposalivation. Thirty-one patients who improved on antidepressant medications have significantly higher pretreatment salivations as compared with 37 patients who did not improve. The salivation rate provides a possible criterion for judging success in treatment on a specific biological basis. Analysis of age, sex, diagnosis, and initial

Clinical Studies
Abstract 3114

severity of depression showed that none decisively alters this relation of salivation rate to improvement.

74 Fenwood Rd.
Boston 15, Mass.

SEE ALSO: 2873, 2877, 2917, 2918, 2924, 2925, 2932, 2941, 2955, 2956, 2957, 2962, 2963, 2967, 2968, 2969, 2970, 2971, 2972, 2973, 2974, 2975, 2977, 2978, 2979, 2983, 2985, 2987, 2990, 3000, 3001, 3006, 3013, 3117, 3118, 3122, 3125, 3137, 3195.

3114 Kaplan, Stanley M., Kravetz, B. Stuart, & Ross, W. Donald. The effects of imipramine on the depressive components of medical disorders. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 1362-1367.

Forty-nine patients, 18 men and 31 women, aged 20-50 years, were treated with 75-500 mg imipramine/day. Observational approaches included double-blind, single-blind and open observations. Patients were selected for evidence of overt depression, evidence of experiencing object loss and indication that the patient's adaptive measures had failed and the response was rather passivity, helplessness, and restlessness. Greater interaction with the environment, decreased depression and decreased physical manifestations of disease were noted. Some beneficial results were obtained in 42 out of the 49 patients.

Dept. of Psychiatry
University of Cincinnati
Cincinnati 29, Ohio

SIDE EFFECTS

3115 Medical World News. SOS poison. Medical World News. 1962, 96, 311-315.

The Poison Centre at the Fernand Widal Hospital, Paris, offers a 24-hour telephone service on poison information which has already saved countless lives. Treatment rooms supplement the telephone service, with a trained staff of specialists. Of 250 coma cases treated in 1 year's time, 96% recovered. Complete blood transfusions are used for patients afflicted with delayed action symptoms to prevent further damage. Patients in barbituric coma recover best when placed under close supervision without administration of an antidote. Two similar centers are contemplated in Nancy and Lyons. (No refs.)

[No address]

3116 Noack, Charles H. An unfortunate effect from the ill-judged self-administration of chlordiazepoxide ("Librium"). Medical Journal of Australia, 1962, 1, 930-931.

Chlordiazepoxide was prescribed after meals and in the evenings (10-20 mg.) to be taken depending on the state of tension and anxiety in a 37-year-old male who was severely agitated. He was instructed upon dosage repeatedly but was so intent on ventilation that he did not readily absorb what was said. Two days later after 20 mg. chlordiazepoxide after breakfast, he momentarily lost consciousness and had a minor collision with his car. Tolerance varies greatly from patient to patient and chlordiazepoxide should be prescribed in a dose of no more than 10 mg. thrice daily, preferably after meals. (13 refs.)

Observatory Clinic
Melbourne, Australia

3117 Trethowan, W. H., & Pawloff, Theodore. A clinical and experimental study of bromide intoxication, with special reference to bromureides. Medical Journal of Australia, 1962, No. 7, 229-232.

One-hundred twenty-eight patients seen over a period of $4\frac{1}{2}$ years were admitted to hospitals with psychiatric symptoms with raised serum bromide levels of 50 mg./100

ml. or higher. Thirty-eight patients showed symptoms of acute bromide intoxication; in 48 others, a subacute reaction was observed. In 52 cases, the cause was due to self-medication with proprietary bromureide preparations and in 32 cases, patients had taken a mixture prescribed by a doctor or a pharmacist. In the remaining 44 cases, the source of bromide was doubtful. In 2 experiments observed, serum bromide levels were proportional to the ingested daily dose. Bromides in any form no longer deserve a place in the pharmacopoeia and, by the same token, the sale of proprietary preparations should be restricted. (9 refs.)

University of Sydney
Sydney, Australia

3118 Hodgkinson, Robert. A study of the clinical effects of Catha edulis (khat, miraa) in Kenya. Medical Journal of Australia, 1962, 1, 884-886.

Khat is widely used in Abyssinia, Arabia and East Africa, being an important article of commerce in these areas. It is alleged to be a habituating drug. Continuous chewing over a long period is said to lead to a loss of a sense of reality. Users become listless. No increase in crime is associated with its use. The experience of a European where Khat appeared to be a stimulant causing euphoria, mental stimulation, and anorexia is described. Ten African volunteers were studied; a 20 mm. rise in systolic blood pressure and slight increase in pulse rate were noted. Then a study using 30 male African volunteers was made of preference for Khat, 15 mg. sustained-release capsules of dexamphetamine or placebo. No preference was demonstrated between Khat and dexamphetamine, but both were preferred to a placebo. No effect of Khat is described which cannot be attributed to an amphetaminelike drug. Alles et al. (1961) indicate that the active principle of Catha edulis is dextro-nor-pseudo-ephedrine. (No refs.)

Department of Clinical Investigation
Parke, Davis and Co.
Ann Arbor, Mich.

3119 Friis, Thorkild. Eksperimentelle undersogelser under fenacetinindgift til mennesker. [Experimental examinations after the administration of phenacetin in man.] Nordisk Medicin, 1962, 67, 755.

Sixteen phenacetin-habituated patients with renal insufficiency and 22 cases without renal insufficiency, 11 nonhabituated patients with insufficiency and a fourth group with insufficiency were given phenacetin and determinations of erythrocyte stability were made. The second group had a markedly low erythrocyte stability while the other groups showed normal times. Because impure phenacetin contains acetate-4-chloranilide (0.1%), trials were run with pure and impure phenacetin or nothing in 15 patients. In 9, the time was markedly shortened after pure or impure phenacetin, while it was normal when no phenacetin was given. In 4, time was slightly shortened after impure phenacetin and in 2, normal but markedly shortened after common phenacetin. Phenacetin has a similar effect but not as marked as the impure substance.

[No address]

3120 Hojman, D., Lemberg, A., De Palol, J., & Rubin, B. Estudio experimental de la acción de la iproniazida sobre hígado, miocardio y cerebro. [Experimental studies of the action of iproniazid on liver, heart, and brain.] Revista Clínica Española, 1962, 87, 91-94.

In acute toxicity studies, rabbits received 450 mg/kg iproniazid i. v.; in chronic studies the daily dose was 12 mg/kg p. o. for 30 days. No mortality was noted in the first hour after 450 mg/kg i. v. doses. No pathologic histochemical or histopathological changes in liver or brain were noted. Changes observed included an increase in the number of cases of chronic angiocholitis, lower sinusoidal blood circulation, greater frequency of hydropic degeneration, reduction of chondrioma, and of RNA and of glycogen in hepatocytes. (16 refs.)

Cátedra de Toxicología Facultad de Ciencias
Médicas
Universidad de Buenos Aires
Buenos Aires, Argentina

3121 Jenkins, Margaret Q. Poisoning of the month. Journal of the South Carolina Medical Association, 1962, 58, 400.
[Editorial]

Two boys, ages 4 and 6 years, were admitted in coma following a gasoline sniffing episode. Administration of oxygen resulted in return to consciousness whereupon an extensive history of gasoline sniffing was revealed. (No refs.)

[No address]

3122 Nayrac, P., Lorrain, A., & Arnott, C. Modifications apportées par le traitement à la sémiologie des psychoses maniaco-dépressives. [Modifications in the symptomatology of manic-depressive psychoses brought about by drug therapy.] Lille Médical, 1962, 7, 209-211.

Administration of conventional doses of imipramine to cases of melancholia may completely alleviate the patient's anxiety, confusion, and hypomania. However, confusion may increase at doses higher than 200 mg/day. Hypomania may result independent of the dose, occasionally leading to the mistaken belief that the patient has been cured whereas subsequently suicide may be attempted; i. e., psychotonics are capable of camouflaging the underlying psychosis. Haloperidol, used in the treatment of psychomotor excitation in manic states (at doses of 15-20 mg/day) may trigger, after a period of calmness, excitomotor convulsions which then must be treated with chlorpromazine. Subsequently the patient appears to be in a confused-agitated state. In other patients, an extrapyramidal syndrome appears in which hypertonia is predominant. But psychomotor agitation and logorrhea are suppressed in time, without the underlying condition being affected, and the patient's family is likely to remove him from the institution prematurely. (No refs.)

[No address]

3123 Loiseau, P., Bargues, R., Planques, L., & Cohadon, S. Accidents nerveux dus aux hydantoïnes: aspect électroencephalographique. [Neurologic side effects due to hydantoins: electroencephalic aspects.] *Revue Neurologique*, 1962, 106, 171-176.

Following some accidental changes in the method of manufacture of melantoin, a drug which had hitherto been innocuous, the drug began to trigger some intolerance reactions in some epileptic patients. The factor common to all 4 cases is that of disorganization, but the manner of disorganization is not specific with respect to either patient or drug. Some evidence of intoxication was present however. Cessation of use of the drug resulted in a return of the EEG tracings to a stable and conventional form. (No refs.)

[No address]

3124 Michon, P., Larcan, A., Huriet, C., & Calamai, M. Hépatite mortelle au cours d'un traitement par l'iproniazide. [A hepatitis fatality in the course of iproniazid therapy.] *Bulletin et Mémoires de la Société Médicale des Hôpitaux de Paris*, 1962, 113, 21-23.

Over a 63-day period, a depressed woman, 39 years old, received a total of about 6 g. iproniazid. The first symptoms consisted of nausea, and vomiting, then icterus followed by coma, and eventually death. The autopsy findings were in agreement with those of both viral hepatitis and iproniazid hepatitis. (No refs.)

[No address]

3125 Faure, Henri. Sur les effets activateurs d'un psychotonique en neuro-psychiatrie infantile. Le problème du risque thérapeutique. [On the activating effects of a psychotonic in pediatric neuropsychiatry. The problem of the therapeutic risk.] *Annales Médico-Psychologiques*, 1962, 120, 87-90.

Phaceterane administration in a pediatric clinic resulted in 4 types of reactions: psychic disequilibrium involving cyclical anxiety, and capable of being favorably

influenced by levomepromazine; appearance or reactivation of latent conflict with accentuation of prepsychotic or preneurotic personality traits; fluctuations in psychometric output during medication, but with evidence of the intellectual capacities of the child being observable; diminution or extinction of the scholastic efficiency during medication, but appearance of a new higher level of scholastic efficiency after a period of latency following cessation of the drug. The third phase, i. e., regression to infantile behavior, is frequently marked by violent nightmares and quasihallucinatory pictures of ravishing monsters. Cathartic psychotherapy is aided by the expression of the experiences with the aid of drawings.

Hôpital Psychiatrique
Bonnevall, France

3126 Frankel, Jerome J. Hepatic and renal damage with azotemia associated with iproniazid administration. *American Journal of Gastroenterology*, 1962, 37, 64-69.

A 63-year-old male executive, who had been on long-term anticoagulant therapy because of myocardial infarction had been receiving 10 mg iproniazid/day for 3 months which was increased to 30 mg/day for 5 months. Estimated total intake of iproniazid was 5,480 mg. The patient developed profound azotemia superimposed upon hepatic dysfunction. Complete recovery of both renal and hepatic functions ensued in 33 days of hospitalization. (8 refs.)

Michael Reese Hospital
Department of Medicine
Chicago, Ill.

3127 Trueta, J., & Agerholm, Margaret. Thalidomide-damaged infants. *Lancet*, 1962, No. 7253, 452.

Request is made that cases of congenital limb defect in Britain should be registered as soon as possible after birth with the Nuffield Department of Orthopedic Surgery, Oxford. All cases will be given a code number and personal details withheld. Cooperation of all organizations, official and voluntary, are welcomed and it is

Side Effects
Abstracts 3128-3131

hoped that this move will provide information on the numbers involved. (No refs.)

Nuffield Department of Orthopedic Surgery
Oxford, Great Britain

3128 Dijkhuis, H. J., Hagenbeek, J. H., Bekker, V. V., van Creveld, S., de Monchy, C., & de Jonge, G. A. Thalidomide and congenital abnormalities. *Lancet*, 1962, No. 7253, 452.

A warning was sent out by The Netherlands medical authorities in November, 1961 relating to discontinuation of thalidomide, sold as Softenon, Noctosediv, and Enterosediv. Up to June 27, 1962, 12 cases of malformations in children attributed to thalidomide had been reported, which is limited in view of a population of about 11 million. (No refs.)

Committee of the Dutch Pediatric Society
The Hague, The Netherlands

3129 Rüttner, J. R., Rondez, R., & Maier, C. Chlorpromazin-Ikterus, eine Form der cholestatischen Hepatose. [Chlorpromazine-icterus, a form of choleostatic hepatitis.] *Deutsche Medizinische Wochenschrift*, 1962, 87, 1107-1110.

Fourteen cases of icterus which appeared 5-23 days after administration of chlorpromazine (50-8200 mg. total intake) are reported. Four patients died in connection with pyelonephritis (2), heart failure (1), and nephrosis with uremia (1); the others recovered. One or more liver biopsies were performed in 10 patients. The histopathological hepatic changes observed in biopsy and autopsy material were relatively minor. All cases showed bile thrombi in the biliary capillaries. Formation of thrombi was never pronounced. Liver cells were enlarged, showed loss of glycogen, and sometimes increased lipid content. They contained various amounts of bile in form of droplets or drops. Occasionally, cell necrosis occurred. The hepatic reticuloendothelial cells may also contain bile. No signs of inflammation,

and no accumulation of bile in bile ducts were noted. (9 refs.)

Histopathologisches Institut
Universität Zürich
Zürich, Switzerland

3130 Fisher, Hyman W. Coma due to a combination of barbiturates, scopolamine and dihydroergotamine. *Journal of the Medical Society of New Jersey*, 1962, 59, 500-502.

A 20-year-old woman ingested 99 tablets of Plexonal (45 mg barbitol, 15 mg phenobarbital, 25 mg isobutylallylbarbiturate, 0.08 mg scopolamine and 0.16 mg dihydroergotamine per tablet) after which she was in coma 5 days. This amount is 25 times the hypnotic dose. The course was complicated by convulsions, airway obstruction, phlebitis, bronchopneumonia, anemia, hypokalemia, and hematuria due to anticoagulants. No abnormal physical residuals were observed. (No refs.)

121 East Northfield Road
Livingston, N. J.

3131 Koutsky, Carl D., Mulvahill, John E., & Orbach, Martin W. Danger of depression associated with Rauwolfia therapy. *Lancet*, 1962, No. 82, 346-349.

Rauwolfia drugs induced depression in 8 hypertensive patients, ages 32-70 years, 6 of whom had compulsive personalities and 4 psychotic depression. Onset of depression varied from 2 weeks to 10 months after initiation of Rauwolfia therapy. Rauwolfia compounds utilized included reserpine, Rauwolfia, and alseroxylon. Tranlycypromine and trifluoperazine [dosages unspecified] were administered to combat depression. The use of Rauwolfia drugs should be avoided in depression-prone patients. (8 refs.)

University of Minnesota Medical School
Minneapolis, Minnesota

SEE ALSO 2865, 2866, 2887, 2899, 2934, 2935, 2942, 2943, 2947, 2950, 2976, 2982, 2994, 3003, 3095, 3099.

BEHAVIORAL STUDIES

3132 Molinengo, L. Profil psicofarmacologico del meprobamato. [Psychopharmacologic profile of meprobamate.] Archivio Italiano di Scienza Farmacologia, 1962, 12, 118-129.

Rats were studied with the following schedules: (1) concurrent variable ratio avoidance schedules, (2) guided extinction and (3) simple extinction. The meprobamate dosages, which were administered 1/2 hour before trials, were 0.08, 0.16, 0.24, and 0.32 g/kg. Food motivation was reduced by meprobamate in females more than in males. Meprobamate interfered with right-left discrimination in both sexes. CARs were modified only at the highest doses. Meprobamate produced irreversible modifications in behavior in some cases.

Istituto di Farmacologia e Terapia
Sperimentale
Università di Torino
Torino, Italy

3133 Waller, Marcus B., & Waller, Patricia F. Effects of chlorpromazine on appetitive and aversive components of a multiple schedule. Journal of the Experimental Analysis of Behavior, 1962, 5, 259-264.

Chlorpromazine (30-225 mg sustained released capsules or 25-150 mg b.i.d., p.o.) was administered to 2 male beagles 2 hours before presentation of a multiple schedule (S) with approach-avoidance components (flashing light coupled with food or shock). Chlorpromazine exerted no differential depressing effect. Response rates at low dosages increased slightly on the food reinforced components, while rates on avoidance components remained relatively unchanged. Higher doses resulted in equally depressed response in all components.

Department of Pharmacology
Harvard Medical School
Cambridge, Mass.

3134 Zimmerman, J., & Schuster, C.R. Spaced responding in multiple DRL schedules. Journal of Experimental Analysis of Behavior, 1962, 5, 497-504.

Rats were able to adjust to 2 different

temporal requirements within several multiple DRL schedules of reinforcement and a slight induction between pairs of components was found. Initial administration of 1 mg/kg amphetamine differentially disrupted spaced responding in the components of a multiple DRL 36 DRL 18 schedule, but did not eliminate discrimination between the components. After maximal drug effects, the chronic administration of 0.6 mg/kg amphetamine was accompanied by a progressive recovery of behavior towards the characteristics of saline control.

Indiana University Medical Center
Indianapolis, Ind.

3135 Janssen, Paul A.J., Niemegeers, Carlos J.E., & Verbruggen, Frank J. A propos d'une methode d'investigation de substances susceptibles de modifier le comportement agressif inné du rat blanc vis-à-vis de la souris blanche. [On a method for the investigation of substances able to modify innate aggressive behavior in the white rat against white mice.] Psychopharmacologia, 1962, 3, 114-123.

Killer rats were selected among male Wistar rats for persistent killing of mice. Three dosage levels of drugs were tested s.c.: 160, 80, 40, etc. mg/kg. The dose of an agent inhibiting or abolishing aggressivity in 50% of killer rats (ED 50 in mg/kg s.c.) was calculated by probit analysis (Siegel 1956). In a series of about 300 compounds, none were specifically inhibitory for either aggressiveness or voracity (tendency to devour the victim), without severe catatonia or some other severe behavioral effect. Chlorpromazine, haloperidol, triperidol, haloanisone, perphenazine, morphine, meprobamate, chlordiazepoxide, amphetamine, and hydroxyzine were among the agents tested. In contrast to Karli's (1959) results, hydroxyzine did not modify aggressivity.

Research Laboratorium Dr. C. Janssen
Beerse, Belgium

3136 Flexner, J.B., Flexner, L.B., Stellar, E., de la Haba, G., & Roberts, R.B. Inhibition of protein synthesis in brain and learning and memory following Puromycin. *Journal of Neurochemistry*, 1962, 9, 595-605.

Young adult albino mice were used in a study of cerebral protein synthesis following an antibiotic, Puromycin, given s.c. At various times after Puromycin administration, 0.1 ml of 0.14 M valine $4 \mu\text{C}/30$ g mouse was injected s.c. Intraventricular and combined intracerebral and s.c. injections of Puromycin were also used. Behavior was tested in a 2-compartment hurdle box (grid shock causing the animal to leap the hurdle into the "safe" compartment) and in a Y-maze. Injections of Puromycin suppressed the incorporation of radioactive valine into the protein of several areas of the brain by 83% on the average. This apparent degree of inhibition of protein synthesis, maintained for various periods of time, was without effect on the learning and retention of simple or discrimination avoidance responses. Inhibition of valine incorporation into protein was raised to 95% by combining s.c. and intracerebral injections with Puromycin. However, animals so treated showed disorientation incompatible with learning or memory.

Department of Anatomy
University of Pennsylvania
Philadelphia 4, Pa.

3137 Diethelm, Oskar. Psychotherapeutic interviews and alcohol intoxication. *Quarterly Journal of Studies on Alcohol*, 1962, 23, 243-251.

Psychotherapeutic interviews were taped on 6 occasions for 45 minutes in 23 alcoholics who received saline or 60-70 cc of 95% ethanol i.v. over a period of 18-22 minutes. Blood alcohol levels ranged from 168-190 mg/100 cc after 20 minutes and from 144-122 mg/100 cc after 45 minutes. In 2, blood levels reached 248 mg/100 cc. Toxic behavior varied widely, and was also elicited by placebo infusions in some instances. During the initial 8-10 minutes of acute intoxication, patients spoke with considerable freedom. Revelation of much repressed material was accompanied by subsequent amnesic

episodes pertaining to mention of this material.

Department of Psychiatry
Cornell University Medical College
Ithaca, N.Y.

3138 Wallgren, Henrik, & Sinikka Savolainen. The effect of ethyl alcohol on a conditioned avoidance response in rats. *Acta Pharmacologica et Toxicologica*, 1962, 19, 59-67.

Rats were given 0.4 mg alcohol and the effect of CARs were studied in a 2-compartment shutter box (using electric shocks from a grid floor). Reaction time and number of responses only after shock increased after administration of alcohol, however the CAR was rather insensitive. Major impairment of CARs was only observed when there were overt signs of motor incoordination. After administration of 3 mg/g alcohol outside training sessions every other day for 20 days, diminution of alcohol effect was observed, apparently due to increased tolerance.

Research Laboratories
State Alcohol Monopoly
Helsinki, Finland

3139 Jacob, J. Action analgésique et effets psychotropes de la morphine. [Analgesic action and psychotropic effects of morphine.] *Thérapie*, 1962, 17, 507-518.

In rats, 25 and 50 mg/kg s.c. morphine depresses the avoidance reaction and prolongs exhaustion time in the forced-swim test. At 5 mg/kg maze reaction time is slowed, but errors do not increase significantly until a dose of 25 mg/kg s.c. is reached. The CARs are inhibited at hypoalgesic doses of 7-10 mg/kg.

Institut Pasteur
Paris, France

3140 Faidherbe, J., Richelle, M., & Schlag, J. Nonconsumption of the reinforcer under drug action. *Journal of the Experimental Analysis of Behavior*, 1962, 5, 521-524.

After 5 cats were trained to respond to an auditory stimulus (buzzer) coupled with reinforcement (milk), they experienced alternate sessions in which they received 2 mg methylphenidate s.c. or no drug. On 1 occasion, 2 cats received 6 mg methylphenidate, although they failed to consume the reinforcer (milk). Under normal conditions these 2 animals never ignored the reinforcer. Reinforcement, however, was not essential to produce drug response.

Université de Liège
Liege, Belgium

3141 Sadowski, B., & Longo, V.G. Electroencephalographic and behavioural correlates of an instrumental reward conditioned response in rabbits. A physiological and pharmacological study. *Electroencephalography and Clinical Neurophysiology*, 1962, 14, 465-476.

Male rabbits with chronically implanted electrodes in the hippocampus and thalamus were trained to pull a ring for a food reward at the sound of a buzzer. When the CS was presented the most striking changes were seen in the hippocampal lead in which the synchronous waves increased in amplitude and frequency up to 9 c/seconds. In the period of satiation high amplitude slow waves at 2-3 c/second, intermingled with spindles in the anterior cortex. During the eating period masticatory waves appeared, particularly in the anterior cortex. The CR was very sensitive to cholinergic drugs. Small doses of scopolamine (0.1 mg/kg) abolished but did not interfere with food intake. Eserine restored the performance of the test as well as EEG activation patterns. Chlorpromazine and imipramine exerted a blocking effect only in doses which produced motor disturbances. Amphetamine had 2 effects: in lower doses it facilitated the CR and with higher doses pulling of the ring occurred unaccompanied by feeding. LSD had a similar effect to that of amphetamine in prolonging the performance of the CR. The appearance of masticatory waves was inhibited

by scopolamine, chlorpromazine and imipramine, i.e., by "synchronizing" drugs, as well as by LSD. Amphetamine on the other hand facilitated these waves.

Laboratorio di Chimica Terapeutica
Istituto Superiore di Sanità
Rome, Italy

3142 Dureman, Ingmar, & Scholander, Torkel. Studies in the psychosensory pupillary reflex. II. Habituation after unilateral local application of a sympatholytic agent. *Journal of Psychosomatic Research*, 1962, 6, 55-57.

Thirty-five healthy students, aged 21-23 years, were seated in a comfortable chair in a semi-sound proof room fixating a blinking red light. Pupillograms (psychosensory pupillary reflex) were recorded with a movie camera. After the adaptation period the subjects were exposed to 30 white noise stimuli, given through the earphones. The maximal phasic reaction curve followed the tonic curve, except primarily for the 1st 3 stimuli. Here the tonic curve shows a slow recruitment reaching a maximal level at the 3rd stimulus while the maximal phasic reaction curve is near its maximum by the 1st stimulus and starts declining at the 2nd, suggesting 3 components: tonic activation (prestimulus area), the maximal area of phasic reaction (maximal poststimulus area) and the amplitude of phasic reaction (equal to the difference between maximal post - and prestimulus areas.)

Department of Psychiatry
University of Uppsala
Uppsala, Sweden

3143 DiMascio, Alberto, Rinkel, Max, & Leiber, James. Personality and psychotomimetic drugs. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. *Third World Congress of Psychiatry Proceedings. Volume II.* Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 933-936.

In a double-blind study, 0.07 mg LSD, 500 mg mescaline, 10 mg psilocybin or placebos were given to 18 college students. Nine

"athletic type" (Type A) and 9 "asthetic" (Type B) had been selected through MMPI testing. Before the ingestion of the drugs, psychomotor tasks, learning and mental functioning tests, psychological observations, measures of mood changes and changes in anxiety levels, and the presence or absence of somatic complaints were recorded. Two-and-a-half hours after drug ingestion the battery of 16 tests and psychiatric interviews were repeated. In general, psilocybin tended to produce fewer and milder changes than those of LSD or mescaline. Mescaline produced the most marked alterations. The reactions were a joint function of the drugs administered and personality of the subject; asthetic individuals showed predominantly intellectual and mental alterations, while athletic individuals responded with euphoria and physiological changes.

SEE ALSO: 2931, 3104, 3180, 3181, 3186.

Psychopharmacology Research Laboratory
Massachusetts Mental Health Research Corp.
Boston, Mass.

3144 Schachter, Stanley, & Wheeler, Ladd.
Epinephrine, chlorpromazine, and amusement.
Journal of Abnormal and Social Psychology,
1962, 65, 121-128.

In order to conceal the purpose of the study and the nature of the injection, subjects were told that injections related to the effects of vitamin and vision. Fourteen odd minutes of a slapstick comedy were shown to male college students and evaluation made as to how amusing the film was considered. The 3 injections used were: epinephrine 0.5 cm of a 1:1000 solution s.c., 25 mg chlorpromazine i.m. or placebo s.c. Physical effects were also reported. Epinephrine subjects were more amused than were placebo subjects who, in turn, were more amused than chlorpromazine subjects.

Columbia University
New York, N. Y.

3145 Bajusz, E., Selye, H., & Strebel, R. Neuroleptic phenothiazine derivatives and stress-induced cardiac necroses. In: Cleg-horn, R.A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 924-926.

Neuroleptic phenothiazine derivatives can prevent the development of specific organ-lesions normally elicited by stress. In rats sensitized with a highly active synthetic corticoid, fluorocortisol plus sodium acetate, forced restraint, the trauma of bone fractures, or overdosage with levarterenol--just as a number of other neural and humoral stressors--elicits infarctlike patches of cardiac ne-croses. This type of fatal cardiac damage is prevented by a single dose of 0.5 mg/100 g chlorpromazine and 2.5 mg/100 g cyameproma-zine, injected just before exposure to the stressors. Continuous anesthesia with pento-barbital protected only against the cardiac-necrosis-eliciting effect of restraint, but not against levarterenol and bone fracture. Apparently phenothiazine compounds block some, presumably neural, pathways through which various stressors elicit cardiac lesions.

Institut de Médecine et de Chirurgie expéri-mentales
Université de Montréal
Montreal, Canada

3146 Minakami, Haruhiko, Takagi, Hiromu, & Kobayashi, Shinsaku. Morphine antagonistic actions of N-propargyl-14-hydroxydihydronor-morphinone hydrochloride and related compounds. Life Sciences, 1962, 2, 503-507.

A morphine analogue, N-propargyl-14-hydroxy-dihydronormorphinone HCl, which is equivalent to nalorphine as a morphine antagonist but which produces fewer side effects is reported. The relationship between chemical structure and morphine antagonistic activity is dis-cussed. Two other analogues, more potent than nalorphine but more toxic are also reported. Antagonism was studied in relation to the analgesic action of morphine in mice, in terms of blood pressure and respiration in dogs, electrocorticograms in rabbit and toxicities in mice.

Takamine Laboratory
Sankyo Co., Ltd.
Tokyo, Japan

3147 Gessa, G. L., Costa, E., Kuntsman, R., & Brodie, B. B. Evidence that the loss of brain catecholamine stores due to blockade of storage does not cause sedation. Life Sciences, 1962, 2, 441-452.

Levarterenol and 5HT were assayed in mice, rabbits and rats after various treatments with α -methyl-metatyrosine, (α MMT), α -methyl-metatyramine and α -methyl- β -hydroxyl-met-a-tyramine. The injection of 100 mg/kg α MMT i.v. produced a small transient decline of 5HT and a complete depletion of levarterenol in brainstems of rabbits which lasted 11 days or more. Doses as low as 10 mg/kg almost com-pletely depleted brain levarterenol stores without affecting those of 5HT. None of the animals showed sedation. The action of α MMT was far less prolonged in mice than in rab-bits. Measurements of α MMT amines in rat heart were made. The effects of α MMT and its metabolites on the heart provided confirming evidence against the view that levarterenol is displaced by α MMT-yramines. After hydroxy-MMTA, levarterenol (1 μ g/g) is completely depleted when the level of α MMT-yramines is less than 0.05 μ g. Inhibition of catechola-mines storage by itself does not cause se-dation.

Laboratory of Chemical Pharmacology
NIH
Bethesda, Maryland

3148 Gupta, S. S., Gupta, J. C., & Agarwala, V. Hepato-toxic effects of hydantoin deriva-tives used in epilepsy. Current Medical Practice, 1962, 6, 57-62.

Of 4 groups, of male rats, 1 received no drugs, 1 diphenylhydantoin, 1 phethenglate for 10 weeks. All drugs were administered intragastrically, 10 mg/kg. After sacri-fice, liver secretions were fixed and studied for evidence of hepatotoxicity. Controls revealed no pathological changes. Diphenyl-hydantoin-treated animals showed definite areas of focal necrosis in 40%, although al-leviation was marked in rats receiving con-comitant high protein diets. Phethenglate produced patchy, centrilobular and hemorrhagic necrosis, which was again diminished with a high protein diet. Hepatic damage was ob-served in all animals treated with hydantoin derivatives. Hepatotoxic effects may be minimized, however, by concomitant adminis-

tration of a high protein diet.

Gandhi Medical College
Bhopal, India

3149 Stern, Jack, & Ward, Arthur A., Jr.
Supraspinal and drug modulation of the alpha motor system. Relation of supraspinal and drug modulation to parkinsonism. *Archives of Neurology*, 1962, 6, 404-414.

The modulating effects of supraspinal stimulation and drug administration (pentobarbital, 30 mg/kg, curare or atropine) on the alpha fraction of the motor system were monitored by monosynaptic testing in 49 cats. Facilitation of the alpha motor system is evoked by stimulation of contralateral or homolateral globus pallidus. Alpha facilitation evoked by ventrolateral thalamic or pallidal stimulation is abolished or reversed by barbiturates. Chlorpromazine (1.5-5 mg/kg i.v.) markedly augments alpha motor discharge in intact alpha preparations.

Division of Neurosurgery
University of Washington School of Medicine
Seattle, Washington

3150 Zilberstein, R. Michel. Reserpine and serotonin-estrogen interactions on the uterus of the rat. *Life Sciences*, 1962, 2, 281-283.

Various doses of 5HT and reserpine were administered s.c. daily for 4 days to 24-25 day old Harvard rats and concomitantly they received daily injections of 0.1 μ g estradiol. Autopsy was performed 24 hours after the last set of injections. Estrogen enhanced the effects of reserpine and 5HT. In spite of the fact that food and water were freely available the reserpine-treated group suffered from inanition; the heightened response to estrogen may be due to the phenomenon described by Jailer (1948), i.e., to starvation-induced interference with the normal hepatic detoxification of steroid hormones. Increased sensitivity of the uterus of the estrogen-treated rat to 5HT and heightened uterine response to estrogen in the 5HT-treated animal were parallel.

RFD #2
Manchester, Connecticut

3151 Revzin, A.M., Maickel, R. P., & Costa, E. Effects of reserpine and benzoquinolizines on limbic system excitability, brain amine storage and plasma corticosterone level in rats. *Life Sciences*, 1962, 2, 699-707.

A bipolar recording electrode was stereotactically implanted in the ventral hippocampus of anesthetized male Sprague-Dawley rats. Stimulating electrodes were positioned in the lateral amygdalar nucleus and septal area on the same side as the recording electrode and in the contralateral ventral hippocampus. After a 2-week recovery period the animals were found to yield stable electrical responses for 2-4 months. All drugs were injected i.p. Reserpine (5-10 mg/kg), tetrabenazine (20-40), RO 19564 (100) and benzoquinamide (50) were used. Plasma corticosterone concentrations were measured according to Guillemin et al. (1959). Reserpine and several benzoquinolizines blocked brain amines storage processes, increased hippocampal excitability and plasma corticosterone levels. In contrast, compounds which fail to block 5HT storage have no effect on these indices of CNS function. Reserpine-induced effects on the hippocampus and on plasma corticosterone levels are related to changes in brain 5HT.

Laboratory of Chemical Pharmacology
National Heart Institute
NIH
Bethesda, Maryland

3152 Kuntzman, R., Costa, E., Gessa, G.L., & Brodie, B. B. Reserpine and guanethidine action on peripheral stores of catecholamines. *Life Sciences*, 1962, 2, 65-74.

Reserpine and guanethidine have different modes of action in relation to depletion of levarterenol stores. Levarterenol in rat tissues was assayed spectrofluorometrically and guanethidine colorimetrically at 515 μ m (α -coupling--Sakaguchi reaction for guanethidine groups). After administering 35 mg/kg guanethidine to rats, about 1/2 of the drug disappeared in the 1st hour. After the 2nd hour the rate of disappearance was sharply reduced, and the half-life found to be about 7 hours. Reserpine (0.25 mg/kg i.v.) was also used, and both drugs lowered cardiac levarterenol level at 0.5 hours, 1 and 2 hours after injection. Results were as follows: reserpine, 64, 56, and 31; guane-

thidine, 89, 78 and 49. Sympathetic blocking agents were used and the experiment repeated. Guanethidine releases levarterenol in sympathetic nerve endings by an action which seems different from reserpine, acting oppositely to bretyllium and activates the process involved in the normal release of levarterenol by nerve impulses.

Laboratory of Chemical Pharmacology
National Heart Institute
NIH
Bethesda, Maryland

3153 Kreppel, E. Zur Differenzierung zwischen zentraler und ganglionärer pharmakodynamischer Dämpfung des Sympathicus. [A method for differentiation between central and ganglionic pharmacodynamic inhibitors of the sympathicus.] *Medicina Experimentalis*, 1962, 7, 223-231.

Spontaneous electrical activity was registered from the sympathetic fibers of the hilus of the left kidney of anesthetized cats. Both vagi had been cut and the carotid sinus eliminated. Narcotin (3 mg/kg i.v.) and Phentanyl (10 mg/kg i.v.) produced reduction and cessation, respectively, of the electrical activity. Activity reappeared after asphyxia which stimulates central sympathetic centers. The electrical response at the hilus seen after stimulation of the brachial plexus was not affected by these drugs, while ganglionic blocking agents abolish spontaneous response as well as that induced by asphyxia and plexus stimulation.

Pharmakologische Institut
Rheinische Friedrich Wilhelms-Universität
Bonn, Germany

3154 Kuhn, H. F., & Friebe, H. Die Ausscheidung von Codein und Codeinmetaboliten im Harn codeingewohnter Ratten und Meerschweinchen. [Urinary excretion of codeine and codeine metabolites of rats and guinea pigs made tolerant to codeine.] *Medicina Experimentalis* 7, 1962, 255-261.

Rats and guinea pigs received codeine s.e. 1-3 times daily for 6-9 weeks in increasing amounts, up to 3-5 times the LD 50. Free and bound codeine, morphine, norcodeine and

normorphine were identified in the urine. Amounts of codeine and codeine metabolites, and the ratio freebound codeine were different in the 2 species. Amounts excreted were dependent only on the administered dosage and were not affected by the duration of treatment.

Pharmakologische Institut
Universität Bonn
Bonn, Germany

3155 Estler, C. J., Heim, F., & Strubelt, O. Sauerstoffverbrauch, Körpertemperatur, Futteraufnahme und Metabolitgehalt des Gehirns weisser Mäuse nach Reserpin [Oxygen and food consumption, body temperature, and content of brain metabolites of white mice after reserpine administration.] *Medicina Experimentalis*, 1962, 6, 395-401.

Reserpine (1 µg/g/s.c.) administered to mice maintained at 24°C reduced oxygen, food consumption and body temperature, while raising the glycogen and ATP content of the brain. It reduced brain phosphocreatine and coenzyme A levels but did not affect lactate and ADP content. Most of these changes are found more pronounced at 18°C.

Pharmakologische Institut
Universität Erlangen-Nürnberg
Erlangen, Germany

3156 Arora, R. B., Singh, M., & Kanta, Chandra. Tranquilizing activity of jatamansone--a sesquiterpene from *Nardostachys jatamansi*. *Life Sciences*, 1962, 2, 225-228.

The i.p. injection of an alcoholic extract of root and rhizomes of *Nardostachys jatamansi* in mice showed demonstrable sedative action at 40 mg/kg and above while the LD₅₀ of this extract was 975 mg/kg. The average fall in mean rectal temperature of mice injected i.p. with 10, 30, 100, 300, 1000 mg/kg of jatamansi was 1.5, 5.2, 6.3, 10.6 and 12.6°C respectively. For the study of hypnotic potentiation, 1, 3, 10, 30 and 100 mg/kg jatamansone was injected i.p. into mice, followed by a standard dose of 35 mg/kg pentobarbital i.p. Maximal potentiation and hypnosis (assessed by the righting reflex) was achieved when 35 mg/kg phentobarbital was given 3 hours

after 100 mg/kg jatamansone. Antiapomorphine effect was studied in dogs and 100 mg/kg jatamansone i.p. reduced emesis by 75%. Hostile monkeys were given 100 mg/kg jatamansone i.p., which provided a 75% reduction in excitement, defensive and aggressive hostilities, while sociability and contentment increased by 80%. The i.p. LD 50 in mice is 580 ± 6 mg/kg.

Department of Pharmacology
All-India Institute of Medical Sciences
New Delhi 16, India

3157 Pittman, James A. Antithyroid activity of a tranquilizer. *New England Journal of Medicine*, 1962, 267, 861-864.

Amphenidone possessed antithyroid activity when administered in large doses (0.6 or 1% of the diet by weight) to rats. Goiters developed in the rats and accumulation of I^{131} in the thyroid gland was depressed. Its action is mediated by a block in the thyroidal organic binding of iodide similar to that induced by drugs such as thiourea. The discharge of thyroidal I^{131} in dogs showed that while it was more rapidly accumulated it was not retained and leaked out quickly so that the 24-hour uptake approximated 0. Radioiodide uptake in 7 psychiatric patients after a single dose of 1200 mg showed no change in thyroidal function.

VA Hospital
Birmingham, Alabama

3158 Roath, S., Elves, M. W., & Israëls, M. C. G. Effect of thalidomide on leucocyte cultures. *Lancet*, 1962, No. 7260, 812-813.

Leukocytes from healthy individuals were treated in vitro as follows: controls, 50 μ g/ml thalidomide, 25 μ g/ml thalidomide, 150 μ g/ml phenobarbital and 50 μ g/ml glutethimide. Differential counts were made after 72 hours incubation. Inhibition of the cells was demonstrated only with thalidomide. Results support the suggestion of Hunter (1962) that thalidomide may be a potential antimitotic agent and also indicate that the effects of all new agents on normal cell cultures might be part of a screening program to which these drugs should be subjected.

Department of Clinical Hematology
Manchester Royal Infirmary
Manchester, Great Britain

3159 Dobkin, Allen B., & Israel, Jacob S. The effect of SA 97, perphenazine, and hydroxyzine on epinephrine-induced cardiac arrhythmias during methoxyflurane anaesthesia in dogs. *Canadian Anaesthetists Society Journal*, 1962, 9, 36-41.

The effects of SA 97 (an antihistaminic) perphenazine and hydroxyzine on epinephrine-induced cardiac arrhythmias during methoxyflurane anesthesia in dogs were studied. Pulmonary ventilation was augmented during anesthesia to eliminate hypoxia and hypocarbia during experiments. Perphenazine in a dose of 0.25 mg/kg was more effective than 1 mg/kg hydroxyzine and 1 mg/kg SA 97 in reducing cardiac arrhythmias produced by epinephrine challenge. However none of the drugs completely eliminated serious ventricular arrhythmias. Therefore epinephrine should not be used during anesthesia with methoxyflurane unless a small amount is injected s.c. in a very dilute solution (less than 1:200,000).

Department of Anesthesiology
Upstate Medical Center
Syracuse, New York

3160 Trendelenburg, U., Muskus, A., Fleming, W. W., & Gomez, Alonso de la Sierra, B. Modification by reserpine of the action of sympathomimetic amines in spinal cats; a classification of sympathomimetic amines. *Journal of Pharmacology and Experimental Therapeutics*, 1962, 138, 170-180.

The modification by pretreatment with reserpine (1 or 2 injections of 3 mg/kg each 24 or 48 and 24 hours, before the experiment) of the dose-response curves of 14 sympathomimetic amines was studied in spinal cats. The responses of the nictitating membrane, the blood pressure and the heart rate were recorded. Pretreatment of short duration with reserpine (previously found not to cause supersensitivity to levarterenol) was found to distinguish 3 classes of sympathomimetic amines. 1) Levarterenol-like amines were as potent in reserpine pretreated as in normal preparations and may therefore be regarded

as predominantly direct acting. 2) Tyramine-like amines were less effective after pretreatment with reserpine; the maxima of their dose-response curves were depressed, and this reduction of their maximal response was correlated with the reduction of the response of the nictitating membrane to nerve stimulation. Therefore they may be regarded as predominantly indirect acting. 3) Pretreatment with reserpine shifted the dose-response curves of several amines to the right without affecting their maxima (ephedrine, m-tyramine, etc.). These amines have both direct and indirect actions, and seem to represent a gradual transition from the 1st to the 2nd group rather than a distinct 3rd group. Five pairs of meta-OH and para-OH analogues were studied; all 5 meta-OH compounds had more pronounced direct effects than the para-OH analogues. The position of the phenolic hydroxyl group is of greater importance and the presence or absence of the alcoholic hydroxyl group in the -position of less importance than hitherto assumed.

Department of Pharmacology
Harvard Medical School
Boston, Massachusetts

3161 Roos, Björn-Erik, & Werdinius, Bengt. Effect of reserpine on the level of 5-hydroxy-indoleacetic acid in brain. *Life Sciences*, 1962, 2, 105-107.

Reserpine (2-5 mg/kg) was injected i.v. into rabbits which were killed at 2-48-hour intervals. Analysis of 5HIAA was performed on 2 or 3 pooled brainstems; 5HT was also analyzed. Two hours after the injection of reserpine the value of 5HT in the brainstem had decreased 3% of the normal, while the corresponding value of 5HIAA had decreased 38% above normal. This high level was still found 12 hours after the injection, but after 24 hours the value of 5HIAA was again normal. The increase of 5HIAA values seems to reflect the release of 5HT induced by the drug.

Department of Pharmacology
University of Göteborg, Sweden

3162 Derynacker, A., Theeuwissen-Lesuisse, F., Buu-Hoi, N.P., & Lapière, C. L'anoxie

cérébrale expérimentale; effet protecteur des dérivés di l'acide p-chlorophénoxyacétique. [Experimental cerebral anoxia; protective effect of p-chlorophenoxyacetic acid derivatives.] *Medicina Experimentalis*, 1962, 239-244.

p-Chlorophenoxyacetic acid and 14 of its derivatives were tested for their efficacy in combating nitrogen-induced anoxia in rabbits. Nitrogen was introduced into a Plexiglas box at the rate of 5 liters/minute and the onset of anoxia measured by EEG. The effectiveness of the substances was measured by the activity quotient, i.e., the ratio of pre- and post-perfusion times before the onset of anoxia occurred. p-Chlorophenoxyacetic acid, its bromine and fluorine analogues, and the dimethylaminoethyl ester are equal to or more effective than the acid proper, while the remaining derivatives are inactive or toxic. Modification of respiratory rate does not occur with these compounds.

Institut de Neurologie
Université de Louvain
Louvain, France

3163 Lamarche, Guy, & Patoiné, Jean-Cuy. Propriétés convulsives du diéthylamide de l'acide vanillique. Note préliminaire. [Convulsive properties of vanillic acid diethylamide. Preliminary note.] *Laval Médical*, 1962, 33, 571-575.

Intract curarized cats and encéphale isolé preparations were used in the study of vanillic acid diethylamide (EEG & ECG; average convulsive dose 8 mg/kg up to 40 mg/kg). The compound has marked convulsive properties at doses lower than those usually used with pentetrazol. The convulsive dose varies from animal to animal. Vanillic acid diethylamide acts at all levels of the CNS and produces neuronal hypersynchrony in the brain. Predominance of action at any 1 level has not been demonstrated. Cortical convulsive crises resemble those of pentetrazol, however the frequency of discharges is usually lower.

Département de Physiologie
Université Laval
Québec, Canada

3164 Gordonoff, T. Über die analgetischen Wirkungen von Monoaminoxidase-Hemmern. [On the analgesic action of monoaminoxidase inhibitors.] *Medicina Experimentalis*, 1962, 7, 201-204.

Iproniazid, bromide, nialamide and phenelzine were tested for their analgesic properties in rabbits by the Gordonoff method (1962), and in rats by the Wolff, Hardy and Goudell method. Doses were 25 mg/100 g iproniazide p.o. (rats only) and 50 mg/kg p.o. for all 4 substances in the rabbit experiments. In addition rabbits also received 0.1 mg pyridostigmine s.c. Analgesic effects were significant, especially in the rabbits. Under oral administration, analgesia sets in after 20-40 minutes and lasts for 100-120 minutes. The analgesic effect is however too weak to explain improvement noted in angina pectoris patients when these drugs are administered in terms of MAO activity, and is probably due to psychopharmacologic action.

Laboratorium von Prof. Gordonoff
Medizinische Fakultät der Universität
Bern, Switzerland

3165 Gisset, G. W., & Lewis, G. P. A spectrum of pharmacological activity in some biologically active peptides. *British Journal of Pharmacology*, 1962, 19, 168-182.

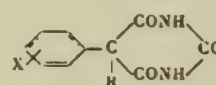
The actions of bradykinin, angiotension, oxytocin, vasopressin and substance P were examined on isolated smooth muscle preparations and in vivo. Isolated rat uterus and guinea pig ileum can be used to distinguish between oxytocin and bradykinin, and isolated rat colon and hen rectal cecum are almost specific test preparations for substance P. All the peptides were active on peripheral blood vessels, bradykinin, substance P and oxytocin causing vasodilation and vasopressin and angiotensin vasoconstriction; bradykinin, substance P and angiotension also caused an increase in capillary permeability in guinea pigs. Only bradykinin and substance P were active in low concentrations in producing pain when applied to an exposed blister base. These two peptides were also active in causing bronchoconstriction. Oxytocin and vasopressin were the only peptides which have milk-ejecting (lactating guinea pig) and antidiuretic activity (rat) which could be dissociated from cardiovascular effects. A possible function for substance P is based

on its vascular and permeability effects.

National Institute for Medical Research
Mill Hill
London N.W. 7
Great Britain

3166 Carissimi, M., Grasso, I., Grumelli, E., Milla, E., & Ravenna, F. Nuovi barbiturici alogenati. [New halogenated barbiturates.] *Farmaco*, 1962, 17, 390-413.

Two series of new barbiturate derivatives have been prepared, whose general formula is:



When R is ethyl or allyl, X in the 4 position can be any halogen, however in 2' and 3' position X can only be chlorine. Acute toxicity and hypnotic properties were studied in mice. Halogen derivatives appeared to have a greater muscle relaxing effect than the parent compounds and they show some effectiveness in protection against electroshock convulsions.

Laboratori Ricerche Maggioni & Co.
Milan, Italy

3167 Efron, D. H. Reserpine toxicity and "nonspecific stress." *Life Sciences*, 1962, 2, 561-564.

Increased toxicity of reserpine in adrenalectomized rats is unrelated to the lack of a pituitary-adrenocortical response and cannot be attributed to a "nonspecific stress." Normal, adrenalectomized and hypophysectomized male Sprague-Dawley rats were used and LD 50's (mg/kg i.w. reserpine) established at 26.4, 18.6 and 0.28 which indicate that the toxicity in adrenalectomized animals is about 100 times greater in intact animals, while in hypophysectomized rats it is only about 1.4 times greater than in intact animals. Increased reserpine toxicity in adrenalectomized rats is related to the absolute lack of certain adrenal steroids which in some way may condition the nervous system to the effect of the drug.

Laboratory of Chemical Pharmacology
National Heart Institute
Bethesda 14, Maryland

3168 George, Robert, Haslett, Wilford L, & Jenden, Donald J. The central action of a metabolite of tremorine. Life Sciences, 1962, 2, 361-363.

The central actions of oxotremorine are described following injection of 50-250 mg/kg into laboratory animals including chickens, pigeons, mice, rats, guinea pigs, rabbits, cats, dogs and monkeys. As it has a marked parasympathomimetic effect when administered alone, it was found desirable to premedicate the animals with methantheline or atropine methylbromide. Tremor, ataxia and spasticity always follows the administration of oxotremorine, which are immediate in mice, rats, and rabbits following i.v. injection. Cats and monkeys, in particular, become markedly excited, pacing, jumping and circling around. This is followed by a ragelike state lasting 20-40 minutes. When rage gradually subsides it is followed by a pronounced fear or withdrawal reaction. Some effects suggested the possibility of hallucinatory experiences. Evidence for CNS action is obvious. Intraventricular injection of a small dose in rabbits produced pronounced tremor. Also transection of the spinal cord in rats at T6 or L1 abolished tremor only below the level of the section. Thirdly, ablation of the midbrain tegmentum prevents tremor in rats while removal of structures rostral to this area did not alter the normal response.

Department of Pharmacology
University of California Medical Center
and Brain Research Institute
Los Angeles, California

3169 Scott, George T. Suppression of melanocyte dispersion in the frog by psychic energizers. Nature, 1962, 193, 552-554. Varying amounts of amphetamine and methylphenidate were injected i.p. into light-adapted frogs. The degree of melanocyte exposure was observed microscopically in the web of the foot and a notation made according to the Hogben and Slome melanophore scale (1931). The percentage of pigment dispersion caused by the drugs was determined by comparison with controls. Similar experiments were carried out with MAO inhibitors (pheniprazine, phenelzine and iproniazid), as well as antidepressants (pipradol, isocarboxazid, nialamide and imipramine). Amphetamine is a potent dispersion suppressor.

Of the MAO inhibitors, pheniprazine was most active, phenelzine intermediate and iproniazid least active.

Department of Biology
Oberlin College
Oberlin, Ohio

3170 Day, M.D., & Rand, M. J. Antagonism of guanethidine by dexamphetamine and other related sympathomimetic amines. Journal of Pharmacy and Pharmacology, 1962, 541-549.

Chloralosed dogs and cats were injected or infused with drugs into a suitable vein. Sympathetic responses were elicited either directly, by stimulating the cervical sympathetic nerve and recording the contractions of the nictitating membrane, or reflexly, by bilateral occlusion of the carotid arteries or by electrical stimulation of the central end of a divided vagus nerve and recording the effects on blood pressure. Dexamphetamine and certain other reacting sympathomimetic amines prevent or reverse the sympathetic nerve blocking action of guanethidine. Levatterenol and dopamine do not antagonize the blocking action of guanethidine. The possession of a reliable and rapidly acting antagonist of bretylium and guanethidine such as dextroamphetamine may extend their use to patients with occlusive vascular disease in whom unpredictable falls in blood pressure are dangerous.

Department of Pharmacology
School of Pharmacy
University of London
Brunswick Square
London, W.C. 1, Great Britain

3171 Dobkin, Allen B., Israel, Jacob S., Criswick, V. Guy. Prolongation of thiopental anaesthesia with hydroxyzine, SA 97, thiethylperazine, and thioridazine. Canadian Anaesthesiological Society Journal, 1962, 9, 342-346.

Four series of crossover experiments were carried out on dogs to establish prolongation of thiopental induced sleep (20 mg/kg thiopental i.v., followed immediately by i.v. injection of the test drug). Percentage increases were: 5 mg/kg hydroxyzine plus 44%, 5 mg/kg SA 97 plus 50%, 0.5 mg/kg thiethyl-

perazine plus 60% and 0.5 thioridazine plus 107%. Hydroxyzine caused prolongation of thiopental sleep but inconsistently, whereas the other 3 drugs invariably delayed recovery.

Department of Anesthesiology
Upstate Medical Center
Syracuse, N. Y.

3172 Perlès, R., & Benda, Ph. Pharmacologie de quelques γ butyrolactones à action centrale. [The pharmacology of some γ -butyrolactones with central action.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. --Annals of Moreau de Tours. Volume I. Current memories in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 374-378.

γ -Butyrolactone at 300-700 mg/kg i.p. causes sleep with loss of the righting reflex in rats for several hours. Onset of action is rapid, i.e., hypnotic effects noted at 10 minutes. At 300-600 mg/kg i.m. in pigeons loss of muscle tonus is noted at 1-3 minutes, lasting 1-2 hours. In rabbits ca. 500 mg/kg γ -butyrolactone i.v. causes an immediate hypnotic effect. Pharmacologic information is presented on α -bromobutyrolactone and 2-dichlorobutyrolactone. These compounds are readily water soluble and may be administered in the form of an emulsion. The action of α -hydroxy- $\beta\beta$ -dimethyl- γ -butyrolactone in pigeons, rabbits and rats (rat i.p. LD 50 700-1200 mg/kg) is discussed.

[No address]

3173 Ernst, A. M. Phenomena of the hypokinetic rigid type caused by O-methylation of copamine in the para-position. Nature, 1962, No. 4811, 178-179.

Carlsson (1958) showed that practically all dopamine in the mammalian brain is found in the caudate and entiform nucleus and that reserpine depletes dopamine from the corpus striatum producing parkinsonism which can be counteracted by DOPA the precursor of dopamine. There is a striking similarity in the chemical structure of dopamine compared to bulbocapnine, papaverine and the drugs laudanosine and laudanine: For example,

laudanine in cats causes a hypokinetic rigid syndrome combined with tremors. Only 1 of the 2 OH groups of the dopamine-ring (I) were changed into OCH_3 groups. Moreover, mescaline (VI) with 3 OCH_3 groups causes a similar hypokinetic syndrome.

Pharmacological Institute
University of Utrecht
Utrecht, The Netherlands

3174 Palomo Salas, T. Études expérimentales et histopathologiques de l'imipramine. [Experimental and histopathologic studies of imipramine] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. Annals of Moreau de Tours. Volume I. Current memories in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 148

Experimentation with fish, guinea pigs, pigeons, cats, mice, rabbits and monkeys was pursued on an acute or chronic basis using imipramine [dosage unspecified]. Pyridoxine neutralized spasms in fish and epileptiform crises in monkeys. Animals sacrificed after chronic intoxication showed diffuse cerebral lesions, including cortical and central nuclear sclerosis. These lesions were observed even in cases where clinical signs were not apparent. In contrast few or slight lesions were noted in a monkey killed in a major seizure by the acute injection of imipramine.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3175 Baruk, H., Launay, J., & Perlès, R. Expérimentation animale du G 22 355 (Imipramine) chez le singe. [Animal experimentation with G 22 355 (Imipramine) in the monkey.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. --Annals Moreau de Tours. Volume I. Current memories in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 144-147.

Imipramine was used in increasing doses (7-40 mg/kg i.m.) in monkeys in order to study psychomotor behavior. Up to 30 mg/kg, a phase of excitation with hyperactivity and

hypersensitivity was noted. The next phase approached catalepsy but was shortly replaced by a stage of muscular weakness progressing to paresthesia with hypotonia, followed by motor incoordination and finally epileptic crisis at 40 mg/kg.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3176 Baruk, H., & Launay, J. Action du chlorhydrate de prothipendyl sur le comportement psychomoteur du Singe. Comparaison avec l'action de la chlorpromazine. [Action of prothipendyl hydrochloride on the psychomotor behavior of the monkey. Comparison with the action of chlorpromazine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie.--Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 136-143.

The activities of chlorpromazine and prothipendyl were compared in monkeys. The catatonic inducing properties of prothipendyl are less than those of chlorpromazine but psychomotor paralysis is manifested very quickly even at low doses. The dosage was 5-35 mg/kg.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3177 Baruk, H. & Launay, J. Experimentation de l'alimemazine in monkeys. Action sur le comportement psychomoteur. Action combinée avec l'imipramine. [Experimentation with alimemazine in monkeys. Action on psychomotor behavior. Combined action with imipramine.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie.--Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 108-112.

In monkeys, alimemazine was used in doses from 5-15 mg/kg i.m., or in combination treatment alimemazine dosage was kept constant at 5 mg/kg and imipramine was used at 20, 30 and 40 mg/kg, all i.m. With alimemazine alone, sedation (light sleep), central motor paralysis

occurred, while no neurological disturbances of the extrapyramidal type were noted. With the combination, imipramine's psychomotor exciting properties were inhibited but its extrapyramidal disorder-inducing faculties were not affected by alimemazine. Psychomotor and neurological disturbances are unrelated phenomena.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3178 Schenker, Anne C., Schenker, Victor J., & Kissin, Benjamin. Aberrations in the pulmonary respiratory pattern in alcoholics and the acute effects of ethyl alcohol and chlorpromazine upon such patterns. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 389-396.

In many alcoholics there is a consistent inability to complete expiratory excursions in the manner requisite for an even baseline on the spirogram. Spirograms were recorded on 101 male alcoholic patients, aged 20-56 years and in 20 nonalcoholic subjects, aged 22-55 years. The alcoholic population was comprised of 56 chronic alcoholic inpatients, 22 alcoholic outpatients and 23 abstainers who volunteered. In acute tests 1 mg/kg of absolute alcohol was given p.o. and led to an apparent alleviation of respiratory irregularity. Parallel tests were run with 4 patients using 25 mg chlorpromazine i.m. Analogously, improvement in respiratory irregularity occurred in 3 of these 4 patients. While there is no evidence to indicate that respiratory irregularity is specific to alcoholism, the spirogram method described is suggested as a testing procedure for assay of drug effects.

Downstate Medical Center
Brooklyn, New York

3179 Stokes, Peter E., & Lasley, Betty. Blood alcohol-kinetics in humans as influenced by thyroid administration or by induced changes in carbohydrate metabolism. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry

Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 385-389.

A series of 91 studies was performed on 26 patients selected from psychiatric wards. Some were diagnosed as chronic alcoholics while others had occasional excessive alcohol ingestion associated with their mental problems. The effect of glucose, insulin and thyroid analogues on blood alcohol disappearance curves were studied. Tests were performed in the fasting state starting in the morning, once or twice a week. The effect of insulin on blood alcohol levels in man is unpredictable, generally small and often absent. Hyper- or hypoglycemia increased blood epinephrine or cortisone do not per se produce any effect on blood alcohol. Triiodothyronine and its propionic and acetic acid derivatives given in pharmacologic doses have no significant effect on blood alcohol curves under the controlled conditions of these studies during the 4-6 hour periods of observation after their administration. There is no striking reproductive clinical effect of insulin, hyperglycemic or thyroid substances on the return to sobriety in the intoxicated persons studied.

Payne Whitney Psychiatric Clinic
New York, New York

3180 Werboff, Jack, & Gottlieb, Jacques S. Behavioural effects of prenatal administration of psychotropic drugs. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal University of Toronto Press and McGill University Press, 1962, Pp. 921-924.

Reserpine, iproniazid, 5 HTP, BAS and distilled water as a control were administered i.p. during the 2nd trimester of gestation from days 8 through 14 to rats. Prenatal treatment had no effect on measures of motor maturation or learning ability. There were changes or reduced weight gain, increased activity and emotionality on the open field test and increased susceptibility to audiogenic seizures (bell alone or pentetrazol and bell). Apparently the psychotropic drugs altered the histochemical action of focalized CNS areas (hypothalamus and reticular for-

mation) to produce a relatively long-lasting functional improvement or detrimental change in behavior. Increased pharmacological technology will one day be able to produce psychotropic drugs with great specificity in site and mode of action so that we might be able to control or improve intellectual or emotional patterns by alteration of the prenatal environment.

Lafayette Clinic
Detroit, Michigan

3181 Heise, George A., & McConnell, Howard. Differences between chlordiazepoxide-type and chlorpromazine-type action in "trace" avoidance. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 917-921.

Chlordiazepoxide (i.p.), meprobamate (i.p.), phenobarbital (s.c.) chlorpromazine (s.c.) and pentobarbital (s.c.) were administered to rats. Rats were trained to respond during the initial noise in "trace" classical avoidance trials consisting of 3 events in sequence: 5 seconds of noise, 5 seconds of silence, 5 seconds of noise and shock (scare boxes containing a lever, loud speaker and a grid scrambler circuit for shocking--automatic recording with an Esterline-Angus Operations Recorder. The dose-response curves and the dose ratios for failure to respond during the 3 events in the trial differentiated between chlordiazepoxide-type compounds, chlorpromazine-type compounds and hypnotics. The distinctive action of chlordiazepoxide-type compounds in trace classical avoidance is interpreted as a shift in latency distribution rather than as a specific block of a secondary CR. The chlordiazepoxide-type compounds in trace avoidance produced the effects reported for chlorpromazine-type compounds in Maffi's (1959) secondary CR situation, while chlorpromazine-type compounds in the secondary CR situation.

Hoffman-LaRoche, Inc.
Nutley, New Jersey

3182 Wilson, S. P., & Tislow, R. Differential antagonism of reserpine eyelid closure by imipramine and amphetamine. Proceedings of the Society of Experimental Biology and Medicine, 1962, 109, 847-848.

In acute studies both 100 mg/kg imipramine and 0.5-4.0 mg/kg amphetamine showed marked antagonism to reserpine ptosis in mice (imipramine 45% and amphetamine 18-63%). Reserpine was injected i.p. at 2.5 mg/kg. Eyelid closure scores were made after Rubin et al. (1957). After the repeated administration of 50-200 mg/kg imipramine/day, appreciable antagonism (7-72%) was still demonstrable, but 4-64 mg/kg amphetamine/day produced only slight antagonism (4-14%). Imipramine was considerably more active than amphetamine in antagonizing eyelid closure in mice.

Wyeth Laboratories Inc.
Research and Development Division
Radnor, Pa.

3183 Vanni, F., & Riggi, F. Étude expérimentale des effets biologiques du Tofranil associé aux inhibiteurs des MAO et aux neuroleptiques, dans les animaux. [Experimental study on Tofranil's biological effects in animals when combined with MAO inhibitors and neuroleptics.] In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 929-932.

EEG's, ECG's and blood samplings for electrolytes were conducted in male adult rabbits before, 7 days and 14 days after treatment with imipramine, chlorpromazine and pheniprazine. The drugs were administered singly or in combinations for 14 days as follows: 10 mg/kg chlorpromazine s.c., 10 mg/kg imipramine i.m., 2 mg/kg pheniprazine i.m. or (same dosages and routes) chlorpromazine plus imipramine, chlorpromazine plus pheniprazine and imipramine plus pheniprazine. Mortality, in the order given above, was 0/10, 2/10, 0/10, 0/10, 6/10 and 7/10. The combination of a phenothiazine derivative with an MAO inhibitor produced brain histopathology, with the combination chlorpromazine-pheniprazine producing the most serious damage. This combination also caused marked sedation and loss of plasma electrolytes. The combination imipramine-pheniprazine was moderately toxic,

having an edemagenic effect on nerve cells producing intense excitation and causing plasma potassium loss. Chlorpromazine-imipramine was nontoxic, though the edemagenic action of imipramine was still present. Chlorpromazine lessened excitation due to imipramine.

Clinica Psichiatrica dell'Università di Milano
Milan, Italy

3184 Sanz Gadea, R. Accion de la clorpromazina sobre la vitamina C en orina de rata y cobaya. [Action of chlorpromazine on vitamin C in the urine of the rat and guinea pig.] Archivo Instituto Farmacologia Experimental, 1962, 26, 61-64.

Guinea pigs were given 300 mg/kg vitamin C/day and rats 100 mg/kg/day along with chlorpromazine as follows: 5, 10 and 20 mg/kg/day for guinea pigs and 3, 6 and 8 mg/kg/day for rats. Only vitamin C was administered for the 1st 10 days followed by its combination with chlorpromazine for the ensuing 10 days. In guinea pigs, chlorpromazine vitamin C excretion was reduced by 40, 46 and 77% in accordance with increasing chlorpromazine dosage. The relevant figures in rats were 21, 23 and 30%.

Instituto de Farmacologia Experimental
Madrid, Spain

3185 Baruk, H., Launay, J., Bergès, & Perlès, R. Action expérimentale de la serotonine sur le comportement psychomoteur du Singe. Antagonisme et synergie avec les neuroleptiques et le L.S.D. 25. [Experimental action of serotonin on the psychomotor behavior of the monkey. Antagonism and synergism with neuroleptics and LSD 25.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie.--Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962. Pp. 275-290.

Intramuscular and i.p. doses of 5HT (5-1000 mg/kg) were used in monkeys. Also doses of 5HT were combined with chlorpromazine and LSD. 5HT did not cause complete experimental catatonia, but induced flaccidity and diminution of initiative in monkeys with exhibition of inquietude, instability and pathetic

attitudes reminiscent to phenomena observable in precatatonic periods. The combinations 5HT-chlorpromazine and 5HT-reserpine showed that 5HT inhibited chlorpromazine effects and increased reserpine effects. 5HT counteracted LSD psychomotor effects. Present knowledge still appears insufficient for proper elucidation of pathogenetic mechanisms of action in regard to these substances.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3186 Baruk, H., & Launay, J. Expérimentation psychopharmacologique de la chlördiazépoxide (R.O. 5-0690) chez le Singe. [Psychopharmacologic experimentation with chlördiazepoxide (RO 5-0690) in the monkey.] In: Baruk, Henri, & Launay, Jacques [Eds.] Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. --Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology. Paris: Presses Universitaires de France, 1962, Pp. 256-259.

Progressive doses of chlördiazepoxide (20-100 mg/kg i.m.) were given to 5 monkeys. Sedative action with slowing of spontaneous activity and a tendency to immobility was noted without catalepsy at 20 mg/kg. Neurological difficulties with incoordination and marked drowsiness was noted at 50 mg/kg, and these manifestations were exaggerated at 75-100 mg/kg, e.g., incoordination in jumping. Chlördiazepoxide appeared only slightly toxic and interest was expressed in its suppression of aggressiveness and fear reactions.

Laboratoire de Psychopharmacologie Expérimentale
Etablissement National de Saint-Maurice
Saint-Maurice, France

3187 Bagdon, R. E. Experimental and clinical toxicology of Librium, a tranquilizing agent. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 915-917.

Chlördiazepoxide toxicity tests were conducted in rats, chickens, dogs (liver function tests), guinea pigs (copulatory reflex) and rabbits

(ovulation). Some rats received amounts 600 times the usual clinical daily dose of 0.5 mg/kg prescribed for man; in these measurements where rats received the drug continuously over the entire life span, chlördiazepoxide was revealed to be an innocuous substance. In dogs 20-60 mg/kg/day produced mild to moderate sedation and animals which received 80 mg/kg displayed gastrointestinal disturbances, some ataxia, and marked sedation and hypnosis for ca. 4-6 hours after each dose. Tests in rabbits and guinea pigs showed the compound devoid of endocrine influence. Additionally suicide attempts with amounts ranging to 1630 mg are reviewed; here toxic reactions were limited to slight ataxia and drowsiness.

Hoffman-LaRoche Inc.
Nutley, N. J.

3188 Schmidt, Joachim & Matthies, Hansjürgen. Über einen zentralen Serotonin-Noradrenalin-Antagonismus. [Central antagonism between serotonin and levarterenol.] Acta Biologica et Medica Germanica, 1961, 7, 107-109.

Experiments with mice showed that the marked potentiating effect on hexobarbital anesthesia (100 mg/kg i.p.) obtained when either 5HT (100nM) or levarterenol (50 nM) was injected into the forebrain alone was abolished and even reversed when the 2 drugs were injected together. Thus, the potentiating effect of 5HT could be reversed by 0.5 nM levarterenol, as well as by dopamine, while the potentiating effect of levarterenol was abolished by 40 nM 5HT. The analeptic effect of injections of 5HT into the hindbrain could also be abolished by simultaneous injection of levarterenol or dopamine, but the reverse in this case was not true.

Pharmakologische Institut
Medizinische Akademie Magdeburg
Magdeburg, Germany

3189 Mougouin, M., & Milovanovich, J. B. Contribution à l'étude clinique et expérimentale en cardiologie de la nialamide ou (pyridinyl 4) 1-phenyl 8-dioxo 1, 6-triaza 2, 3, 7-octane. [Clinical and experimental use of nialamide (pyridinyl-4) 1-phenyl-8-dioxo-1, 6-triaza-2, 3, 7-octane] in cardiology.] Press Médicale, 1962, 70, 1189-1192.

Nialamide action was investigated on isolated rabbit ventricles and guinea pig hearts. At concentrations of 10-50 mg/100 cc of the perfusion liquid, it has a negative inotropic and chronotropic action, and at sufficiently high concentrations (200 mg/100 cc) will cause complete stoppage. Epinephrine is antagonistic to this action. Of 127 cases of coronary angina treated with nialamide, an attenuation of the spasms up to the point where the patients were able to resume light work was recorded in 103 cases, failure was noted in 16; 3 had died because of infarcts and 5 other infarct patients were saved. Side effects include abdominal distension, postprandial tachycardia, paroxysmal tachycardia and constipation all requiring use of adjunct drugs. Tolerance was good; only 2 cases reacted unfavorably to the dose used.

Hôpital Broussais-La Charité
Paris 14, France

3190 Türker, Kazim, & Akcasu, Alaaddin. The effect of morphine on 5HT content of cat's brain. *New Istanbul Contribution to Clinical Science*, 1962, 5, 89-97.

The 5HT level in cat brain is 2.63 to 0.553 μ /g in the diencephalon and 0.8 to 0.55 μ /g in the frontal lobes. Morphine (1-6 mg/kg s.c.) induced 5HT depletion in the frontal lobes and, to a lesser extent, in the diencephalon. With 1 mg/kg morphine, a sharp decrease in 5HT level, was evident, whereas less depletion occurred with 3-6 mg/kg doses. Diencephalon 5HT levels were 1/3 that in normal preparations 24 hours after morphine administration, whereas frontal lobe levels were approximately normal. No linear relationship

was observed between dose and depletion. No direct correlation could be determined between morphine effects and 5HT level.

Department of Pharmacology and Therapeutic Clinic
University of Istanbul
Istanbul, Turkey

3191 Baruk, H., & Launay, J. Expérimentation psychopharmacologique animale du S. 1544 (phénelzine). [Animal psychopharmacologic experimentation with S 1544 (phenelzine).] In: Baruk, Henri, & Launay, Jacques [Eds.] *Annales Moreau de Tours. Tome I. Mémoires récents sur la psychopharmacologie. --Annales of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.* Paris: Presses Universitaires de France, 1962. Pp. 229-233.

The pharmacology of phenelzine in dogs, cats and particularly monkeys, guinea pigs, mice and pigeons is outlined. Psychomotor excitation with hyperactivity and hypersensitivity to stimuli is evident at low doses (10-120 mg/kg). In mice the i.p. LD₅₀ is 168 mg/kg compared to an oral LD₅₀ of 156 mg/kg. At high doses hypotonia, motor incoordination and ataxia are evident sometimes associated with generalized epileptic crises. It is less epileptogenic than imipramine.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

SEE ALSO 2909, 2910, 2911, 2912, 2913, 2914,
2922, 2929, 2930, 2953, 3038, 3081, 3136, 3141

3192 Gessa, G. L., Costa, E., Kuntzman, R., & Brodie, B. B. On the mechanism of norepinephrine release by α -methyl-metatyrosine. *Life Sciences*, 1962, 2, 353-360.

Various test substances were injected i.p. or i.v. into Sprague Dawley rats and levarterenol (norepinephrine) levels were determined according to Shore & Olin (1958). After injection of 400 mg/kg α -methyl-metatyrosine (α MMT), the stores of levarterenol in brain and heart were depleted for a period of more than 24 hours. α MMT reached a peak in the brain within 1 hour and thereafter its level fell rapidly so that in 5 hours it was no longer detectable. To determine the part played by α MMT in releasing levarterenol, rats were pretreated with the decarboxylase inhibitors, NSD 1034 or NSD 1024 and then injected with α MMT. After this pretreatment, α MMT is not converted to the corresponding amine and does not release levarterenol in heart and brain. α MMT acts only through the decarboxylation product.

Laboratory of Chemical Pharmacology
National Heart Institute
Bethesda, Maryland

3193 Brodie, B. B., Kuntzman, R., Hirsch, C. W., & Costa, E. Effects of decarboxylase inhibition on the biosynthesis of brain monoamines. *Life Sciences*, 1962, 2, 81-84.

Even after 5HTP/DOPA decarboxylase in brain is almost completely blocked, 5HT and dopamine are still formed. Therefore, inhibition of this enzyme does not seem to offer a promising approach in the search for agents that block the formation of monoamines. Male NIH general-purpose mice were treated with N-(3-hydroxybenzyl)-N-methylhydrazine (NSD 1034) injected into the tail vein (6.25-200 mg/kg). To block MAO, the inhibitor N-methyl-N-benzylpropynylamine was injected i.p. in doses of 100 mg/kg. Doses of NSD 1034 (6.25-mg/kg) which inhibited decarboxylase by 75% had no effect on the rise of 5 HT and dopamine after blockade of MAO; with doses that blocked the enzyme almost completely, the levels of 5 HT and dopamine still rose by 50%.

Laboratory of Chemical Pharmacology
National Heart Institute
Bethesda, Md.

3194 Street, Harold V. The rapid separation of drugs and poisons by high temperature reversed phase paper chromatography. 2. Phenothiazine tranquilizers and imipramine. *Acta Pharmacologica et Toxicologica*, 1962, 19, 312-324.

Rapid separation of 8 phenothiazine tranquilizers and imipramine occurs during reversed-phase chromatography with aqueous solvents on ester-impregnated paper at temperatures between 85-95°C. The effects of R_f values of a) type and amount of ester, b) pH and concentration of solvent and c) different temperatures have been studied. A modified Marquis reagent and other developing reagents containing concentrated sulphuric acid are described for direct use on the ester-impregnated paper. Time required for ascending chromatography is 20 minutes and for circular chromatography 40 minutes. Blood and urine extracts were sampled.

Department of Forensic Medicine
University of Edinburgh
Edinburgh, Scotland

3195 Berry, Helen K. Use of micromethod for phenylalanine in management of phenylketonuric patients. *Clinical Chemistry*, 1962, 8, 172-173.

Blood is collected in capillary tubes and sealed. The tubes are centrifuged and then the sera from several tubes combined. In a small conical test tube, 0.20 ml 95% ethanol is added to 0.050 ml serum (or plasma) to precipitate protein. The supernatant is drawn into a 50- μ l pipet and carefully applied to filter paper. Quantitative estimations of phenylalanine in serum can be made by comparing the density of ninhydrin color obtained (solvent butanol-ethanol-water;

70-20-20) with known amounts of phenylalanine. The sera from normal and phenylketonuric individuals can be differentiated visually.

Children's Hospital Research Foundation
Cincinnati 29, Ohio

3196 Horita, A., & Weber, L. J. Dephosphorylation of psilocybin in the intact mouse. *Toxicology and Applied Pharmacology*, 1962, 4, 730-737.

Male mice were injected i.p. with 100 mg/kg psilocybin or 72 mg/kg psilocin (equimolar amounts- 0.35 mM/kg). The administration of psilocybin results in the accumulation of its 4-hydroxy analogue, psilocin in the kidney, liver and brain. Highest concentrations in kidney and liver were found within 10-20 minutes and brain levels reached a peak at 25-30 minutes after administration of psilocybin. Behavioral effects, characterized by piloerection, exophthalmos and motor incoordination, closely followed the increase in brain levels of psilocin. In mice pretreated with large doses of sodium β -glycerophosphate, a substrate of alkaline phosphatase, the administration of psilocybin resulted in much lower increases of tissue psilocin levels and behavioral effects were attenuated. The accumulation of tissue psilocin after administration of psilocin did not differ significantly in control or β -glycerophosphate-pretreated mice. Correspondingly, no difference in intensity of behavioral effects was noted. Evidence is presented for the rapid dephosphorylation of psilocybin in the intact mouse and its CNS effects are exerted only after its transformation to its analogue psilocin.

Department of Pharmacology
School of Medicine
University of Washington
Seattle, Wash.

3197 Wilson, Irwin, B., & Alexander, J. Acetylcholinesterase: reversible inhibitors, substrate inhibition. *Journal of Biological Chemistry*, 1962, 237, 1323-1326.

Kinetic measurements show that reversible inhibitors of acetylcholinesterase have a non-competitive component. The correct explanation of substrate inhibition is that the

dealkylation of the acetyl enzyme is prevented by a binding of a molecule of acetylcholine. These findings are consistent with deduction arising from the intermediate formation of an acetyl enzyme in enzymic hydrolysis, as it should be possible to inhibit the dealkylation and this introduces the non-competitive component. Reversible inhibitors are shown to inhibit the hydrolysis of methylcarbamyl enzymes, a reaction analogous to the hydrolysis of acetyl enzyme. Acetylcholine inhibits the hydrolysis of the methylcarbamyl enzyme and, therefore, would be expected to inhibit the hydrolysis of the acetyl enzyme. This would produce substrate inhibition.

Department of Neurology
College of Physicians and Surgeons
Columbia University
New York, N.Y.

3198 Huszak, I., & Durko, I. The metabolism of the indole compounds in schizophrenia. In: Cleghorn, R. A., & Roberts, C. A. *Third World Congress of Psychiatry Proceedings*. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 674-676.

The urinary excretion of 5HIAA by schizophrenic patients and normal subjects using the colorimetric method of Udenfriend et al. (1955) was studied with and without tryptophan loads. When tryptophan loads were applied the number of chromatographic spots did not increase in either schizophrenics or controls and the 5HIAA spot did not enlarge. However in controls the spots corresponding to indoleacetic acid (not 5HIAA) got larger on the days when tryptophan loading was applied, while in the schizophrenics the tryptophan load scarcely influenced the indoleacetic acid excretion. In about 2/3rds of the urines from schizophrenics, a moderately intense pink spot could be detected at 0.07-0.10 Rf values with Ehrlich reagent which was soluble in ethanol and not observed in the controls. The spectrum of this material was found between 210-220 m μ with a maximum at about 205 m μ , which suggests an indole compound.

[No address]

3199 Jackim, Eugene, & Wortis, Joseph. Metabolic abnormalities in mongolism: respiratory activity and triiodothyronine uptake of erythrocytes. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 667-670.

Mongoloid erythrocytes tended to show high oxygen-sugar uptake values as measured manometrically; they also showed a slightly increased lactic acid output and a reduced ability to convert inorganic phosphorus to organic phosphate. The mean phosphorylation-oxidation ratio in mongoloids was 0.077 compared with 0.131 in normal controls. Standard radioiodated triiodothyronine was used in the in vitro RBC uptake test of Hamolsky, Golodetz and Freedberg (1957). Twenty-three control individuals and 22 mongoloids were used as erythrocyte donors. Triiodothyronine uptake increase was consistent and significant for the mongoloids. The mean for the control groups was 50.4 while for the mongoloid group 22.9. Qualitatively both the mongoloid and control sera appeared to bind thyroxine in both the albumin and globulin fractions. Increased triiodothyronine uptake by mongoloid erythrocytes probably is due to an abnormality in serum fraction that binds thyroid hormone and not to the erythrocytes per se. The test is based on a competitive uptake of triiodothyronine between several serum proteins and the erythrocytes. Electrophoresis did not show either a quantitative or a qualitative abnormality in 1 or more of the mongoloid serum fractions.

Jewish Hospital of Brooklyn
Brooklyn, N. Y.

3200 Haddad, R. K., & Rabe, Ausma. An anaphylactic test for abnormal antigen(s) in schizophrenics' serum. In: Cleghorn, R.A., Moll, A.E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 658-661.

Malis and Rybas (1959) reported an abnormal factor in the serum of chronic schizophrenics discovered through challenge to sensitized guinea pigs. This report corroborates their work. The volume, route and time sequence of

sensitizing, desensitizing and challenging injections were patterned after those described. The degree of anaphylactic reaction to challenging injections was weighted on a scale ranging from 0 to 4+. The symptoms rated were nose scratching, sneezing, coughing, convulsions and death. Pooled sera from 12 male schizophrenics who had been hospitalized 2-6 years was used. Thirty-six guinea pigs were sensitized with a 1-10 ml s.c. injection of the pooled sera and 3 weeks later an s.c. desensitizing injection of 0.5 ml serum (similarly pooled) from 18 male nonpatients was used. Two animals were injected for each of the nonpatients. Twenty-four hours later 1 animal of a pair was challenged intracardially with 0.15 ml serum from the same nonpatient, and the 2nd animal challenged with pooled patient serum. This type of experiment was repeated with sera from other schizophrenics, alcoholics and normal patients. Finally the abnormal antigenicity was shown to be common to the sera of schizophrenic patients in different hospitals.

Bureau of Research in Neurology and Psychiatry
Princeton, N. J.

3201 Bogoch, Samuel. Nervous system glycoproteins in mental disorders. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 634-638.

This paper is one of a continuing series of studies on the possible relationship of psychological to biochemical events in the psychoses. Schizophrenic, affective and mixed psychotic disorders are included among 33 cases studied and reported on here. Added to 24 previously reported cases, results on a total of 57 are discussed here. The age range is from 17 to 61 and all cases have been selected at random. Since some of the cases represent multiple admissions, a total of 75 instances of improvement, worsening or no change are reported. In seventy out of seventy-five instances there was correlation between neurochemical changes and the clinical status. In those showing improvement there was an increase in glycoprotein hexose, glycoprotein hexosamine and glycoprotein neuraminic acid, while for definite worsening the

glycoprotein content of the CSF dropped. Whether the accumulation of hexoses and hexosamine precursors bound to protein with a failure of accumulation of neuraminic acid (derivative) represents some form of enzymatic block in biosynthesis, and whether the correlation of this disturbance might be accompanied by clinical improvement is a question for further study.

Neurochemical Research Laboratory
Department of Psychiatry
Harvard Medical School
Cambridge, Mass.

3202 Heath, Robert G., Leach, Byron E., & Byers, Lawrence W. Taraxein: recent developments in processing and identification. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 619-624.

Three possible compounds are referred to: taraxein, a small molecule, taraxein binding protein (TAR B.P.) and taraxeinogen, a small molecule plus a protein. Standard assay was made with rhesus monkeys prepared with chronically implanted electrodes in subcortical structures. The fraction tested is rapidly injected i.v. into the monkey. If the fraction contains taraxein, the monkey developed catatonia and typical EEG changes, unlike the shocklike reaction with stupor waves seen on the injection of either normal or schizophrenic serum. Fractionation of taraxeinogen (protein) included chloroform-alcohol extraction, chloroform-alcohol followed by DEAE cellulose chromatography, DEAE cellulose batch and chromatographic column, batch DEAE cellulose treatment followed by extraction with various phosphate buffers and phosphate buffer fractionation. Fractionation for taraxein (small molecule) involved the following 5 variations: serum pretreated at pH 2 and precipitated with alcohol; serum pretreated at pH 2, incubated with trypsin for 2 minutes followed by alcohol precipitation; pretreated serum at pH 2 and incubated with trypsin for 20 minutes; pretreated serum at pH 2, incubated with trypsin for 3 minutes followed by Retardion column, and pretreated serum at pH 2, incubation with trypsin for 20 minutes followed by Retardion column.

Views are presented on the relation between the protein molecule and the small molecular substance as they relate to the fluctuating symptomatology of schizophrenia.

Tulane University School of Medicine
New Orleans, La.

3203 Fischer, Roland & Griffin, Frances. Biochemical-genetic factors of taste-polymorphism and their relation to salivary thyroid metabolism in health and mental retardation. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 542-547.

The distributions of quinine and 6-n-propylthiouracil taste-thresholds for 37 parents of mongoloids and 48 normal subjects were established. At least one of the parents in each couple or, in twelve out of eighteen pairs of parents of mongoloids, both parents are very high quinine tasters.

Colombus Psychiatric Institute and Hospital
Colombus, Ohio

3204 Smith, W. James, & Kirshner, Norman. Mechanism of 3,4-dihydroxyphenylethylamine- α -hydroxylase. Journal of Biological Chemistry, 1962, 237, 1890-1891.

3,4-Dihydroxyphenylethylamine- β -C¹⁴, H³ was converted to levarterenol α -C¹⁴, H³ by beef adrenal chromaffin granules and by an enzyme isolated from the banana plant (dopamine hydroxylase). The H³:C¹⁴ ratio of the isolated 3,4-dihydroxyphenylethylamine indicating that an α , β -dehydrogenation-hydration mechanism is not involved in the conversion of 3,4-dihydroxyphenylethylamine to levarterenol.

Department of Biochemistry
Duke University Medical Center
Durham, N. C.

3205 Gyermek, Laszlo, & Bindler, Elliot.
Action of indole alkylamines and amidines on
the inferior mesenteric ganglion of the cat.
*Journal of Pharmacology and Experimental
Therapeutics*, 1962, 138, 159-164.

Several indole compounds related to 5HT were found to have marked action on the inferior mesenteric ganglia of the cat. Methylation of the terminal N atom of 5HT maintained or increased ganglionic stimulation dependent upon the number of methyl substituents. N-Dimethylation of tryptamine definitely increased ganglionic stimulant potency as compared to the weak activity of tryptamine. The stimulant action of some of the N methylated compounds (bufotenidine, N,N,N-trimethyltryptamine) was, however, not 5HT-like, but rather of the cholinergic type. N,N-Diethyl and di-n-propyl derivatives of tryptamine and N,N-dipropyl 5HT were considerably weaker than the corresponding N,N-dimethyl compounds. Methylation of the 5OH group of 5HT or altering its ethylamine chain by methyl substitution, or both, brought about marked loss of ganglionic stimulant and blocking potencies. 4- and 6-hydroxy indole alkylamines were inactive on the inferior mesenteric ganglion as compared to 5HT and bufotenine. Introduction of an amidine group in the molecules of tryptamine and 5HT resulted in compounds which primarily blocked the action of 5HT. Marked divergence between the ganglionic and smooth muscle stimulant actions of these agents was demonstrated.

Geigy Research Laboratories
Ardsley, N. Y.

3206 Koella, Werner P., & Schaeppi, Ulrich.
The reaction of the isolated cat iris to
serotonin. *Journal of Pharmacology and Ex-
perimental Therapeutics*, 1962, 138, 154-158.

The effect of 5HT (serotonin) and a number of other substances was tested on the isolated intact cat iris and on the isolated iris sphincter and dilator muscle. The reaction of the pupillary opening on the intact iris was recorded by means of a photoelectric technique. The reaction of the isolated muscles was measured by means of ("isometric") mechanoelectric transducers. The isolated iris reacted to 5HT with miosis. Concentrations of 0.3 μ g/ml of Ringer solution were

effective. The pupillary constriction and ensuing dilation lasted up to 15 or more minutes. Two-peak patterns occurred often with larger doses. 5HT treatment desensitized the preparation to later injections of 5HT. The isolated constrictor muscle reacted to 5HT with contraction and the dilator strip, with relaxation often followed by contraction when larger doses were used. Epinephrine and levarterenol induced dilation of the pupil. Levarterenol led to contraction of the dilator muscle. Atropine had only small influence on 5HT reactions but in moderate doses eliminated acetylcholine effects on the intact iris and the constrictor muscle completely.

Laboratory of Neurophysiology
Worcester Foundation for Experimental
Biology
Shrewsbury, Mass.

3207 Abbs, E. T. The acute sensitization of tissues by choline 2,6-xylyl ether (TM 10), bretylium and guanethidine. *Life Sciences*, 1962, 2, 99-103.

The effect of TM 10 (the bromide), bretylium tosylate and guanethidine as well as epinephrine and levarterenol were studied in vitro on O-methyl transferase derived from rat and cat livers. Supernatants containing both O-methyl transferase and a methionine-activating enzyme were prepared. Concentrations of test drugs varied from 25 g/ml to 1.25 mg/ml. Recovery of synthetic metanephrine added to incubation mixtures containing inactivated enzyme varied from 46.5 - 57%, but was constant in any one experiment. Pyrogallol was used as a reference substance. TM 10 (choline 2: 6-xylyl ether bromide), bretylium tosylate, guanethidine sulphate have been shown to have no significant effect in vitro on the activity of COMT from rat and cat liver, using epinephrine and levarterenol as substrates. The sensitization to epinephrine and levarterenol which these drugs produce in vivo is unlikely to be due to inhibition of the biotransformation of the amines by O-methyl transferase.

Department of Pharmacology
University of Leeds
Leeds, Great Britain

3208 Gheorghiu, P., Schwartz, Rita, Stroescu, V., & Popescu, E. Influentarea compozitiei proteice a creierului prin clorpromazina. [The influence of chlorpromazine on the protein composition of the brain.] *Studii si Cercetari Fiziologice*, 1962, 7, 361-366.

Rats were treated with 1-50 mg/kg chlorpromazine s.c. for 15 days and sacrificed. Trichloroacetic acid precipitates of brain tissue were hydrolyzed and the amino acids analyzed, using descending paper chromatography (ninhydrin). Chlorpromazine induced an increase in the amounts of glutamic acid and alanine. In view of the importance of glutamine and GABA, it is possible that at the central action of chlorpromazine is related to an increase in the amount of glutamic acid available in the brain.

Institutul de Fiziologie Normală si Patologica "D. Danielopolu"
Academiei R. P. R.
Bucharest, Romania

3209 Whittaker, V. P. Sub-cellular distribution of 5-hydroxytryptamine in guinea pig brain. *Nature*, 1962, 195, 1100.

5HT in guinea pig brain is localized in the presynaptic vesicle containing nerve-ending fraction, and the dense type of storage particle found in the duodenum does not occur in this brain. These conclusions were reached by Whittaker in 1959, but disputed by Inouye, Kataoka and Shinagawa (1962). The latter workers inferred that previous 5HT assays had been interfered with by substance P. However, substance P was probably present at the low threshold concentrations, is relatively inactive with rat fundus strip, and the work has been corroborated by Baker (1959) and others.

Biochemistry Department
Agricultural Research Council
Institute of Animal Physiology
Babraham College
Cambridge, Great Britain

3210 Briseid Jensen, Kjell, & Vennerød, Anne Marie. Pharmacological and chromatographic differentiation between a secondary kinin from human urine and bradykinin. *Acta Pharmacologica et Toxicologica*, 1962, 19, 337-334.

Biological effects of urinary kinin and bradykinin were studied on stimulation of the isolated rat uterus, isolated guinea pig uterus, relaxation of isolated rat duodenum and rat blood depressor effect. Chromatographic study of urines was made using the method of Briseid, Jensen & Vennerød (1962) and a secondary kinin not identical to bradykinin was demonstrated. Rat uterus, guinea pig ileum, or rat blood pressure tests distinguished between the substances, but parallel assays with rat uterus and rat duodenum failed to discriminate.

Biological Department
Pharmaceutical Institute
University of Oslo
Oslo, Norway

3211 Creveling, Cyrus R., Daly, John W., Witkop, Bernhard, & Udenfriend, Sidney. Substrates and inhibitors of dopamine- β -oxidase. *Biochimica et Biophysica Acta*, 1962, 64, 125-134.

Dopamine- β -oxidase not only affects the hydroxylation of dopamine to levarterenol, but accepts as substrates a wide variety of phenethylamine derivatives such as epinine, m-tyramine and their branched -methyl derivatives, m-methoxytyramine, which is converted to normetanephrine, 3,5-dimethoxytyramine, and to some extent even mescaline. The fact that many well-known sympathomimetic drugs are good substrates for the enzyme raises the possibility that compounds such as amphetamine, pargederinol, paradrine and α -methyl-m-tyramine owe some of their activity to the corresponding metabolites which are all derivatives of ephedrine. The nonspecificity of dopamine- β -oxidase prompted a search for competitive or specific inhibitors. Benzylhydrazine, isosteric with phenethylamine, inhibited the enzyme strongly at concentrations of 10^{-5} M.

NIH
Bethesda, Md.

3212 Suwa, N., Yamashita, I., Ishikane, M., Owada, H., Shinohara, S., & Nakazawa, A. Fluctuations of the autonomic and endocrine functions in mental disorders. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 839-841.

Day by day estimations of some indices of autonomic and endocrine functions were made on about 50 mixed patients for several weeks to 6 months. BMR, adrenocortical function (circulating eosinophils, urinary 17-ketosteroids, 17-hydroxy-ketosteroids and uropepsin), gonadal function indicated by estrogen and pregnandiol were estimated. Seven case histories are given. Conclusions drawn were: changes in autonomic and endocrine functions are not strictly parallel to emotional changes, but are related; changes in these indices are not specifically related to a disease entity; these biological changes represent attempts at maintaining homeostasis; when homeostasis cannot be preserved as in deteriorated schizophrenics, fluctuations in this function are extreme, and longitudinal observation will aid in integrating contradictory results so far reported by those investigators holding different viewpoints.

Hokkaido, Japan

3213 Kaelbling, Rudolf, Craig, James B., & Pasamanick, Benjamin. The association of hepatic porphyria with mental illness -- the screening of 2,500 psychiatric patients for urinary porphobilinogen. In: Cleghorn, R.A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 624-630.

This study was performed in a 125-bed intensive-treatment hospital. During a 46-month period the Watson-Schwartz test was performed on 2,126 consecutive admissions. Repeat Watson-Schwartz tests were made routinely on readmission of former patients. Of the total 2,500 psychiatric patients examined for porphobilinogenuria, 626 were readmissions. Porphobilinogenuria was considered to mean that Ehrlich-aldehyde reacting substances were

found in the urine of all probands and the purple color which was developed was assumed but not proven due to porphobilinogen. Only 12 of the 35 probands had a clinical picture of acute intermittent porphyria. Nine more were considered to have latent porphyria, 13 secondary porphobilinogenuria and 1 mixed porphyria. Rates of selected clinical manifestations found in probands and controls as well as exposure to possible precipitating factors with comparisons of probands and controls was made. Possible precipitating agents were: chronic alcoholism, addiction to barbiturates, addiction to narcotics, sulfonamid treatments and estrogen treatments. Routine Watson-Schwartz test for all psychiatric patients is advocated.

Tulane University School of Medicine
New Orleans, La.

3214 Jensen, Knud, & Osterman, Einar. Glutamic-oxalacetic transaminase in cerebrospinal fluid in patients with cerebral atrophy. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 607-609.

Fifty controls and 46 patients, including 34 cases of presenile dementia and others (e.g., manic-depressive psychosis and schizophrenia), were tested for GOT content in the CSF. In the 34 cases of presenile dementia the average age was 59.4 years. The duration of the disease was 1-12 years. In 44 cases, cerebral atrophy was demonstrated by pneumoencephalography and in 2 cases by autopsy. In cerebral atrophy, the value in Karmen Units was 11.7, $s=3.56$. In 1 patient an increased GOT content in the CSF was noted while no pneumoencephalographic alterations indicating cerebral atrophy were found. However, when pneumoencephalography was repeated after a 1/2 year, signs of central atrophy were found. In the diagnosis of cerebral atrophy, the determination of CSF GOT content is a valuable aid.

State Mental Hospital
Risskov, Denmark

3215 Yamashita, M. Histopathological studies of the brain tissues of four patients of alcohol delirium. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 396-398.

Histopathologic signs in 4 patients (alcoholic delirium) were relatively acute changes in the diencephalon and the mesencephalon. Examination of blood vessels, especially capillaries and precapillaries revealed endothelial hypertrophy. Neuronophagia, small necrotic lesions and changes in blood vessels in the thalamus, hypothalamus, central nucleus, semilunar nucleus, periventricular gray matter, mammillary body, quadrigeminal bodies and reticular nucleus are evident. The pathogenesis of delirium is considered due to indirect and relatively acute malnutrition and circulatory disturbance of the cerebral blood vessels in chronic alcoholism. Hallucinations in alcoholic delirium is elementary, simple, real and sensory, and shows diencephalic microorganic characteristics. This type of hallucination is termed diencephalic hallucination.

Osaka Kaisei Hospital
Kitakti, Osaka
Japan

3216 Kinross-Wright, John, & Ragland, James B. Clinical pharmacology of some newer phenothiazine analogues. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 901-905.

Determination of blood drug levels with tranquilizers should offer at least some help in evaluating their relative merits. Endeavor in this area has been relatively unrewarding and possibly current studies at the cellular level will be more rewarding. Notes are presented on 4 psychochemical series: phenothiazines, iminodibenzyls, thioxanthenes and dibenzocycloheptanes. Imipramine, chlorprothixene, TX 35, amitriptyline, cyclobenzaprine, cyproheptadine and other agents are discussed. A method for

the determination of phenothiazines based on fluorescence when the compounds are oxidized in acetic acid is described. Fluorescence measurements are made in a spectrofluorometer following basic extraction of the drugs from blood or other samples with heptane, which is then extracted with acetic acid; this allows determination of blood concentrations down to ca.1 $\mu\text{g/ml}$ whole blood, and sometimes even lower concentrations, e.g., 0.05 $\mu\text{g/ml}$ blood thioridazine. All work in this area indicates that blood levels in no way reflect tissue concentrations which are of paramount importance in evaluation. In rats, tissue levels of thioridazine, trifluoperazine and chlorpromazine after i.p. injection lead to the following: 1) all 3 drugs are very rapidly taken up since intracellular concentrations exceed blood levels in 2 minutes; 2) highest concentrations are invariably found in the lungs and liver, as much as 20 times those in other tissues (brain tissue usually has one of the lowest concentrations); 3) levels of thioridazine in brain appear to be consistently lower than those of the other 2 drugs relative to other tissues; 4) thioridazine shows little variation in concentration in different brain areas other than a very small but consistent excess in the thalamus and hypothalamus, and 5) ultracentrifugal fractionation of brain homogenates has shown that thioridazine is restricted to the microsomal fraction and is not found in other particulates or in the supernatant.

Baylor University College of Medicine
Waco, Texas

3217 Rey, J. H. A study in the relationship of hormones, brain activity, and behaviour in women suffering from mental illness. In: Cleghorn, R. A., Moll, A. E., & Roberts, C.A. Third World Congress of Psychiatry Proceedings. Volume II. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962. Pp. 830-832.

Fluctuations in mood, onset of depression and/or schizodepressive episodes were related

to the menstrual cycle and excretion of 17-ketosteroids and rise in the cornification index in 4 women.

Maudsley Hospital
Camberwell, London
Great Britain

3218 Sourkes, Theodore L., Murphy, Gerard F., & Chavez-Lara, Beatriz. Experimental and clinical studies of anti-decarboxylases. In: Cleghorn, R. A., Moll, A. E., & Roberts, C. A. Third World Congress of Psychiatry Proceedings. Volume I. Toronto/Montreal: University of Toronto Press and McGill University Press, 1962, Pp. 649-653.

The excretion of α -methyldopa and a metabolite α -methyldopamine was followed in 3 normal males and 10 psychiatric patients. The drug was administered both i.m. and p.o. in acute and chronic experiments, e.g., 0.75-10 g/day. Only when smaller amounts of α -methyldopa were administered could both the amino acid and its amines be determined in the urine. α -Methyldopa did not significantly change behavior or thinking in the patients, however there are good reasons for retaining an interest in antidecarboxylases as possibly useful agents in clinical medicine aside from α -methyldopa's antihypertensive action.

Worcester Foundation for Experimental
Biology
Shrewsbury, Mass.

3219 Bodur, Hatice, Alatas, Sevda, Sisli, Ceyhan, & Sisli, Tomris. A study on protein-bound hexoses during insulin coma. New Istanbul Contribution to Clinical Science. 1962, 5, 79-88.

Total protein, serum albumin and globulin, and the amount of protein bound hexoses were determined and the amount of hexoses in protein calculated during and after insulin coma of 19 schizophrenics. The amount of insulin used was 100-540 U. No significant differences were detected in the parameters studied.

Departments of Biochemistry and Psychiatry
Faculty of Medicine
University of Istanbul
Istanbul, Turkey

3220 Briggs, Michael H., & Harvey, Natalie. Urinary metabolites of aromatic amino acids in schizophrenia. Life Sciences, 1962, 2, 61-64.

The urinary metabolites of 15 schizophrenic patients, 12 non-schizophrenic psychiatric patients and 18 normal subjects were studied. An abnormality in tyrosin metabolism is indicated in schizophrenia. The metabolic abnormality is explained as a partial inhibition of p-hydroxyphenylpyruvate oxidase due to suboptimal amounts of ascorbate.

Victoria University
Wellington, New Zealand

3221 Antebi, R. N., & King, J. Serum enzyme activity in chronic schizophrenia. Journal of Mental Science, 1962, 108, 75-78.

Twenty-six cases of chronic schizophrenia, including 15 females, were assayed for the following serum enzymes. The serum activities of 9 enzymes, SGOT, SGPT, lactate dehydrogenase (LDH), malate dehydrogenase (MDH), isocitrate dehydrogenase (ICD), pseudocholinesterase (pCE), aldolase (ALD), alkaline phosphatase (ALP) and leucine aminopeptidase (LAP) were measured. Two cases, 1 in remission, showed simultaneous elevated pCE and ALP activity; 1 patient had concomitantly elevated ALP and ICD levels and another ALP and LAP activities. One patient had a high ALP level and 3 had elevated pCE activity. No symptoms of other disease were evident in any of these patients showing abnormal enzyme levels and it is difficult to offer an explanation of these findings as there was no correlation between serum enzyme abnormality and clinical state or age. Estimation of any of the enzymes studied holds no diagnostic value in chronic schizophrenia.

Moorhaven Hospital
Ivybridge, Devon
Great Britain

3222 Levine, Walter G., & Peisach, J. Studies on the substrate specificity of ceruloplasmin. Biochimica et Biophysica Acta, 1962, 63, 528-529.

For each substrate, V_{max} expressed as $\mu\text{l O}_2$ consumed per h per μg ceruloplasmin CU, was plotted semilogarithmically against the sum

of Hammett sigma values for all ring substituents. The more reactive compounds are those with the more highly negative sigma values. Thus a reaction rate of 835 was obtained for p-phenylenediamine with a total sigma value of -1.320, while m-phenylenediamine, with a total sigma value of -0.322 gave a reaction rate of only 39. Compounds having substituents with high positive sigma values showed little or no activity. Although o-phenylenediamine was readily oxidized, 4-nitro-o-phenylenediamine did not react. Similarly, the reaction rate with hydroquinone was 285, while 2,5-dihydroxybenzoic acid, the carboxyl analogue, showed only very slight activity. An increased ring electron density in the substrate is associated with increased activity with ceruloplasmin and it is apparent the enzyme binding may not be through the amine or phenolic groups, but instead directly to the ring, or more specifically, to the π electrons of the ring.

Department of Pharmacology
Albert Einstein College of Medicine
Yeshiva University
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3223 Long, R. F., & Lessin, A. W. Inhibition of 5-hydroxytryptamine uptake by platelets in vitro and in vivo. *Biochemical Journal*, 1962, 82, 5P. [Abstract]

A large number of organic bases inhibited uptake of 5HT by ox blood platelets in vitro, in platelet enriched plasma. Inhibition was competitive and could be reversed by washing the platelets. Active compounds included chlorpromazine, chlorprothixene, imipramine, cocaine, ibogaine, α -methyltryptamine, harmaline, amphetamine, benzylhydrazine, pheniprazine. Benactyzine, caffeine, mescaline, salicylic acid, N-benzyl-N-methylpropyne, pentobarbital, dimethylaniline and iproniazide were only slightly active or were inactive. 5-Hydroxy- α -methyltryptamine was taken up by ox platelets the same as 5HT, and this uptake inhibited competitively by α -methyltryptamine. Concentrations for 50% inhibition of uptake by imipramine ranged from 8×10^{-7} M using human platelets, to 4×10^{-5} M using bovine platelets. Cat platelets were the most sensitive to the inhibitory action of

methyltryptamine, 50% inhibition of uptake occurring at 3×10^{-6} M whereas to produce equivalent inhibition using guinea pig platelets, a concentration of more than 10^{-4} M was required. In these studies 5HT was estimated fluorimetrically.

Research Department
Roche Products Ltd.
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Great Britain

3224 Ruscak, M. Changes in the level of α -aminobutyric acid (GABA) in the ischaemic brain of rats following application of some stimuli evoking spreading EEG depression. *Physiologia Bohemoslovenica*, 1962, 11, 192-198.

In rats, stimuli evoking spreading EEG depression lead to a significant increase in brain GABA content only if bilateral ligature of the carotid arteries was performed concomitantly. The ligature itself however did not affect brain GABA nor the ratio of glutamic acid to GABA in the course of 30 minutes. Local application of 0.3 M and 3M KCl onto the brain as well as mechanical stimuli caused a significant rise in GABA content of the brain cortex. Following 30 minutes applications of 0.3 M KCl, GABA content increased by 41.6%, after 30 minutes application of 3 M KCl by 65.1% and after mechanical stimulation by 31.1% as compared with the GABA content in the hemispheres of control rats. A tracheal ligature of 150 seconds duration also led to an increase of GABA in the cortex by 88.5%. Since the brain GABA content was raised even after stimuli which do not evoke spreading EEG depression, the increase of GABA in the ischemic brain is not specific for EEG depression. This increase in GABA is considered the result of increased utilization of free amino acids in the brain, GABA's formation being increased and its oxidation slowed.

Institute of Experimental Medicine
Slovak Academy of Sciences
Bratislava, Czechoslovakia

3225 Michaux, R. Action catatonigene de la 5-methoxytryptamine. [Catatonic action of 5-methoxytryptamine.] *Life Sciences*, 1962, 2, 617-619.

Intracisternal injections of 25 and 50 μ g 5-methoxytryptamine and 50 μ g 5HT were made in rats. 5-Methoxytryptamine caused intense catalepsy which decreased slowly so that 72 hours after injection, psychomotor inertia was still evident. 5HT rats showed the same symptoms but 48 hours later animals recovered spontaneous activity. The i.p. injection of 700-1400 μ g 5-methoxytryptamine to 140 g rats does not effect their behavior. Methylation of the indole OH 5HT does not suppress its catatonic action; methylation lengthens the action of the drug.

Université de Liège
Département de Biochimie
Laboratoire des Isotopes
Liege, Belgium

3226 Bernheimer, H., Birkmayer, W., & Hornykiewicz, O. Verhalten der Monoaminoxidase im Gehirn des Menschen nach Therapie mit Monoaminoxidase-Hemmern. [Monoaminoxidase in the human brain after therapy with monoaminoxidase-inhibitors.] *Wiener Klinische Wochenschrift*, 1962, 77, 558-559.

Determination of MAO activity were carried out in the nucleus caudatus, cortex cerebri and renal cortices of deceased normal humans, patients with Parkinson's disease, and patients with Parkinson's disease who had been pre-treated with MAO inhibitors. The manometric method was used. High enzyme activity could be measured in the tissues of "normal" controls and "untreated" patients with Parkinson's disease. No significant differences were observed in these 2 groups. In pre-treated Parkinson patients, MAO in the kidney was inhibited to a high degree and brain MAO was completely inhibited.

Pharmakologische Institut
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Vienna, Austria

3227 Kveder, S., Iskric, Sonja, & Keglevic, Dina. 5-Hydroxytryptophol: a metabolite of 5-hydroxytryptamine in rats. *Biochemical Journal*, 1962, 85, 447-449.

Radioactive 5HT (2.26 μ c/mg) was injected i.p. into rats (2.9 mg/100 g). A phenolic eluate from urine was subjected to paper chromatography and autoradiographs studied. A radioactive area with R_f 0.25 was eluted and rechromatographed, resolving into individual peaks with R_f 0.22 and 0.476. The latter, metabolite C, was eluted again and hydrolyzed for further identifications. 5-Hydroxytryptophol was identified as 5HT metabolite. Then the metabolism of 1'-N-acetyl-5-hydroxytryptamine and 5-hydroxytryptophol in rat-liver slices was studied. The former compound remained mainly unchanged (80-90%), whereas 60-70% of 5-hydroxytryptophol was metabolized, being partly oxidized to 5HIAA and partly conjugated. 1'-N-Acetyl-5-hydroxytryptamine and 5-hydroxytryptophol were chromatographically indistinguishable but only the latter was shown to be a metabolite of 5HT. A scheme for the metabolism of 5HT is suggested above. A major metabolite of 5HT excreted in rat urine is a 5-hydroxytryptophol-O-glucuronide. The chemical synthesis of 5-hydroxytryptophol is described.

Tracer Laboratory
Institute Rudjer Boskovic
Zagreb, Yugoslavia

3228 Marquillo, Carlos L., Esperbén, Maria T., & Lasalvia, Eduardo. Variation of pyruvic acid in enzymatic inhibition of monoamine oxidase. *Chemotherapia*, 1962, 4, 580-585.

Blood and urine specimens from 10 normal subjects were analyzed to determine pyruvate and lactate variations before and after administration of nialamide (100 mg/day), Tersavid (1-pivaliol-2-benzyl-hydrazine, 45 mg/day) and Nardelzine (fenelzine-beta-phenylethylhydrazine, 45 mg/day). All patients showed sizeable increases in pyruvate blood and urine levels, i.e., the MAO inhibiting properties of the drugs resulted in the increased pyruvate levels.

Departamento de Investigación Clínica
Hospital Pasteur
Montevideo, Uruguay

3229 Mall, G. Sur la toxicité de la bile et du sérum chez les épileptiques et les schizophrènes. [On the toxicity of bile and serum from epileptics and schizophrenics.] In: Baruk, Henri, & Launay, Jacques (Eds.) Annales Moreau de Tours. Tome I. Mémoires reconts sur la psychopharmacologie. [Annals of Moreau de Tours. Volume I. Current memoirs in psychopharmacology.] Paris: Presses Universitaires de France, 1962. Pp. 349-352.

Bile from normal subjects and schizophrenics was injected into mice (1 ml i.p.) in order to determine sedative, cataleptic and lethal effects. With control bile mortality was 10.9% compared to 43% for schizophrenic bile. No catatonia occurred in mice treated with normal bile, while 17% became catatonic with experimental bile. With control bile 89.1% were asymptomatic compared to 41% for schizophrenic bile. Serum samples from 46 healthy controls and 41 epileptics were hydrolyzed and 1 ml aliquots injected i.p. into mice. Fresh serum was mixed with 2% trypsin in a proportion of 4:1 and incubated for 16 hours at 37°C before use. Results below apply to epileptic sera taken in the attack phase. Mortality was 40.4% for epileptic sera and 11.7% for control sera.

Société Moreau de Tours
Maison Nationale de Charenton
Paris, France

3230 Zmorski, Tadeusz. Aktywność fosfatazy zasadowej w surowicy krwi w przebiegu leczenia schizofrenii chlorpromazyną. [The activity of alkaline phosphatase in plasma during treatment of schizophrenia with chlorpromazine.] Roczniki Akademii Medycznej im. Juliana Marchlewskiego w Białymstoku, 1961, 7, 57-63.

Alkaline phosphatase activity in the plasma of 49 schizophrenics (26 men and 23 women), under prolonged chlorpromazine treatment, was assayed. The highest daily dose of chlorpromazine averaged 327 mg and was given for 36 days. On the average treatment lasted 77 days. Determinations of phosphatase activity were made at 7 day intervals, Bodansky's method being employed. The activity of phosphatase was found unchanged in 36 patients, slightly increased in 10

(an average of 0.7 Bodansky U), and decreased in 3 (0.5-1.0 Bodansky U). Apart from a moderate increase in blood sedimentation rate, no side effects were observed. While no liver damage was indicated by alkaline phosphatase testing, great care is advocated in the administration of chlorpromazine, and liver function should be assayed before and after treatment.

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SEE ALSO: 2881, 2884, 2901, 2908, 2915,
2926, 2954, 2965, 2966, 2986, 2988, 3017,
3021, 3029, 3147, 3173.

ABBREVIATIONS

α -KG	α -ketoglutarate	GABOB	γ -amino- β -hydroxybutyric acid
AACL	Zuckerman's Affect Adjective Check List	HD	hypnotic dose
ACTH	adrenocorticotrophic hormone	5HIAA	5-hydroxyindoleacetic acid
ad lib.	free choice	5HT	5-hydroxytryptamine
ADP	adenosinediphosphate	5HTP	5-hydroxytryptophane
A.M.	morning		
AMA	American Medical Association	i.a.	intraarterial
Art.	Article	ibid.	in the same place
ATP	adenosinetriphosphate	i.e.	that is
		i.m.	intramuscular
BAL	British antiLewisite	IMPS	Lorr's Inpatient Multidimensional Psychiatric Scale
BAS	benzyl analogue of serotonin	i.p.	intraperitoneal
b.i.d.	twice a day	IPAT	Cattell's Institute for Personality & Ability Testing Anxiety Scale
BOL	bromolysergic acid diethylamide	I.Q.	intelligence quotient
BUN	blood urea nitrogen	IU	international unit
		i.v.	intravenous
C	Celsius scale		
ca.	about	kg	kilogram
CAR	conditioned avoidance response	K _i	Michaelis constant for an inhibitor
CBS	chronic brain syndrome	K _m	Michaelis constant for a substrate
cc	cubic centimeter		
CD	convulsive dose	lbs	pounds
cm	centimeter	LD	lethal dose
cm ²	square centimeter	LSD	lysergide
cm ³	cubic centimeter		
C.N.R.S.	Centre National de la Recherche Scientifique	μ	micron
CNS	central nervous system	μ c	microcurie
COMT	catechol-o-methyl transferase	μ g	microgram
cps	counts per second	μ l	microliter
CR	conditioned reflex (response)	μ M	micromolar
CS	conditioned stimulus	m μ	millimicrons
CTD	Climbing Time Delay	M	molar
		ma.	milliamperes
DDT	dichlorodiphenyl trichloroethane	MACC	Motility Affect Cooperation Communication
DOPA	3, 4-dihydroxy-phenylalanine	MAO	monoamine oxidase
DPH	diphosphopyridine nucleotide	MAS	Taylor Manifest Anxiety Scale
DPNH	reduced diphosphopyridine- nucleotide	meq	milliequivalents
		ml	milliliter
ECG	electrocardiogram	mm	millimeter
Ed.	editor	mm ²	square millimeter
ED	effective dose	MMPI	Minnesota Multiphasic Person- ality Inventory
EDTA	ethylenediaminetetraacetic acid	MSRP	Multidimensional Scale for Rating Psychiatric Patients
EEG	electroencephalogram		
e.g.	for example	N	normal
ERG	electroretinogram	NEFA	nonesterified fatty acid
et al.	and others	NIMH	National Institute of Mental Health
etc.	and so forth		
		p	probability
F	Fahrenheit scale	PAH	para-aminohippuric acid
FFA	free fatty acid		
g	gram		
GABA	γ -aminobutyric acid		

PBI	protein-bound iodine	SRA	Science Research Associates
pH	negative logarithm of the hydrogen ion concentration	Suppl.	supplement
P _i	inorganic phosphate	TAT	Thematic Apperception Test
P.M.	afternoon and evening	TH	thyroid hormone
p.o.	by mouth	t.i.d.	thrice a day
ppm	parts per million	TPN	triphosphopyridinenucleotide
PRP	Psychotic Reaction Profile	TPNH	reduced triphosphopyridine-nucleotide
q.i.d.	four times a day	TSH	thyroid-stimulating hormone
refs.	references	U	unit
R _f	ratio of the distance of dissolved substance to solvent distance	UR	unconditioned response
RNA	ribonucleic acid	US	unconditioned stimulus
ru	rat unit	USAF	United States Air Force
s.c.	subcutaneous	USDHEW	United States Department of Health, Education, and Welfare
S.D.	standard deviation	USP	United States Pharmacopoeia
SGOT	serum glutamic oxaloacetic transaminase	USPHS	United States Public Health Service
SGPT	serum glutamic pyruvic transaminase	UV	ultraviolet
sic	exactly as found	VA	Veterans Administration
SOSAI	Springfield Outpatient Symptom and Adjustment Index	viz.	namely
		WAIS	Wechsler Adult Intelligence Scale
		WPRS	Wechsler Psychiatric Rating Scale

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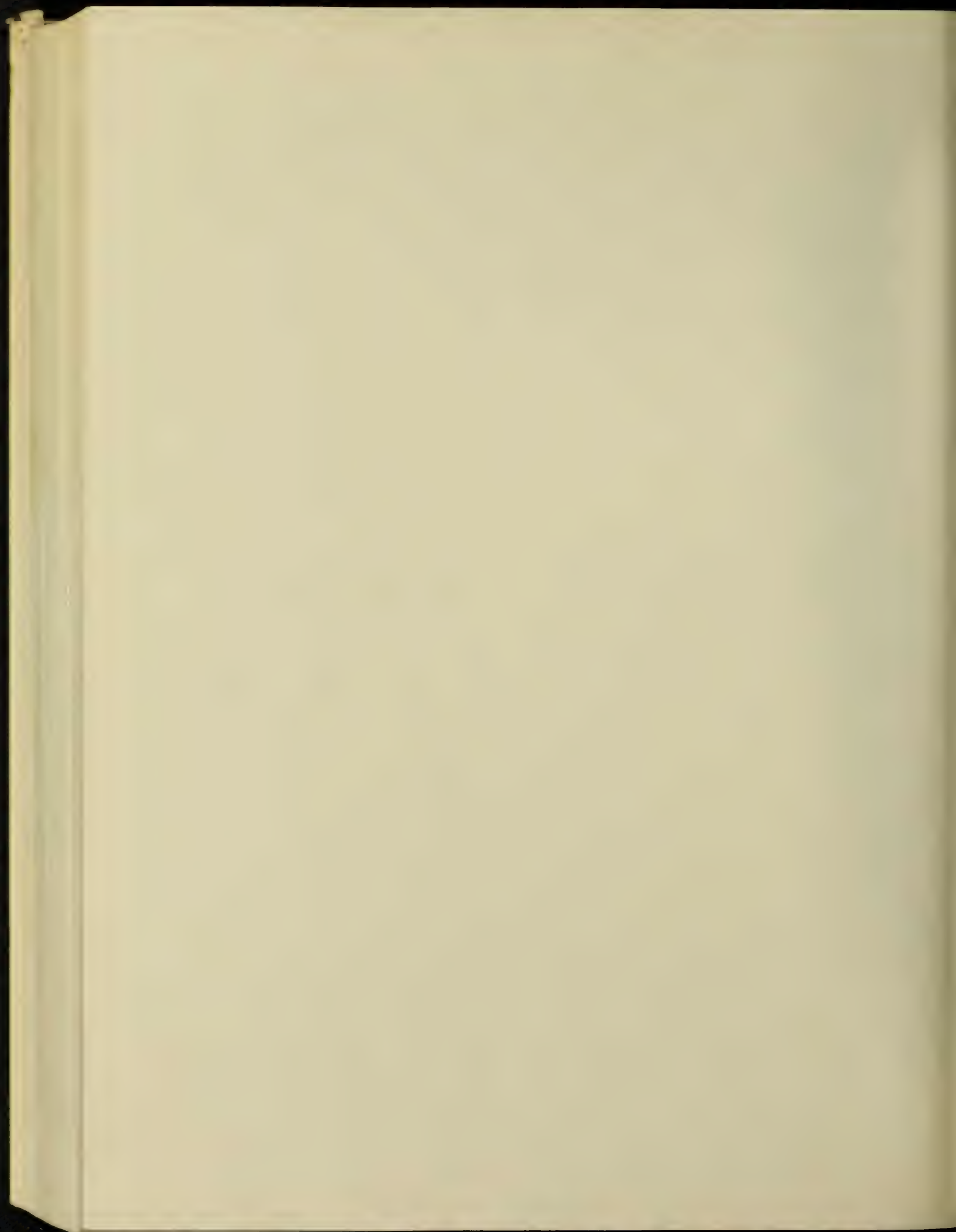
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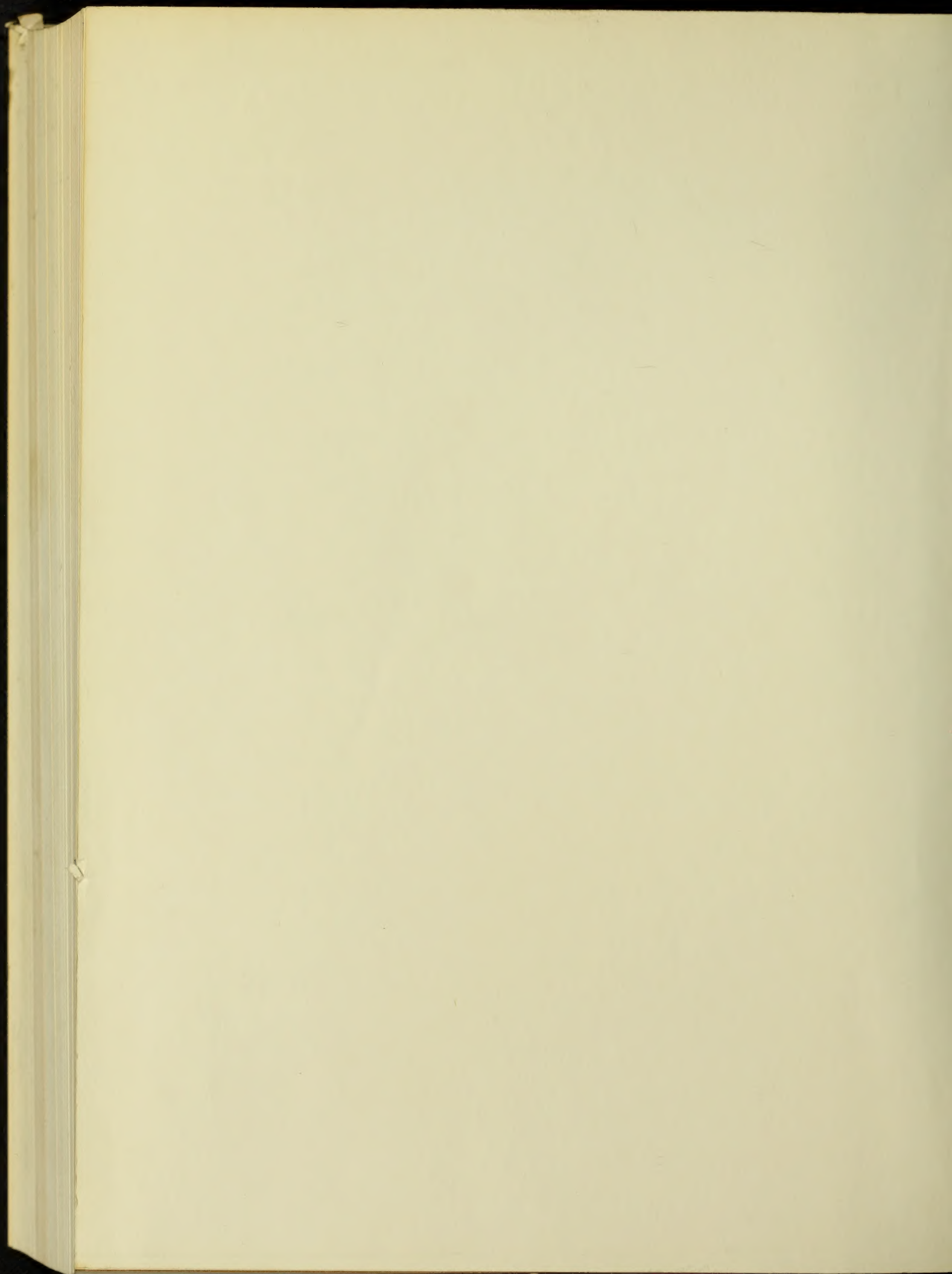
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